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ARCHIVES OF SURGERY

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EFFECT OF FUNDUSECTOMY ON THE ACIDITY OF THE GASTRIC AND DUODENAL CONTENT

AN EXPERIMENTAL STUDY

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Most surgical procedures for treatment of peptic ulcer are used in an endeavor to cause reduction in gastric acidity or in the length of time the ulcer is exposed to the gastric content. These results are brought about either by increasing the speed with which the stomach empties or by causing mixing of the alkaline duodenal sections with the gastric content through an altered or artificial stoma. In all probability few, if any, of the procedures employed affect directly the secretory mechanism involved in the production of hydrochloric acid. It would seem more logical in uncomplicated cases to perform some procedure which would reduce the ability of the stomach to produce hydrochloric acid. With this hypothesis in view experimental work was carried out on dogs in an effort to determine what effect removal of varying portions of acid-secreting mucous membrane has on the acidity of the gastric and duodenal content.

Anatomically the important structures of the stomach intimately concerned with secretion of gastric juice are the nerves and the glands. The innervation is through the vagus and the sympathetic nerves, but, as has been shown by Pavlov,[1] the vagus nerves contain the fibers which are important in the initiation of secretion of acid. The action of the sympathetic fibers is not so well understood, although the recent work of Baxter [2] indicates that the fibers are concerned with the production of alkaline mucus.

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An abridgment of a thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery.

1. Pavlov, I. P.: The Work of the Digestive Glands, London, C. Griffin & Company, Ltd., 1910.

2. Baxter, S. G.: Influence of Splanchnic Nerves on Gastric Secretion, Proc. Soc. Exper. Biol. & Med. **29**:511 (Jan.) 1932.

Histologic observations on the dog's stomach have been made by several investigators. Lim [3] recently found that the fundus comprises most of the stomach and that the cardiac and pyloric regions, with their mucus-secreting glands, are relatively small. In distinction to the structure of the mucosa of the stomach of man, oxyntic cells were found in both the cardiac and the pyloric region, although in the latter they were small and primitive.

These observations have been verified physiologically by the use of pouches made in various portions of the stomach. Pavlov [1] and other investigators repeatedly have demonstrated that the fundic portion secretes acid, while Ivy and Oyama [4] have shown by a similar technic that the secretion of the pyloric region is mucoid and slightly alkaline.

Resection of the acid-secreting mucous membrane in an attempt to reduce gastric acidity was tried by Mann.[5] He reported that in dogs, by diversion of the secretion poured into the duodenum, he could produce peptic ulcers which developed much more slowly and which became indurated more than usual if he removed most of the fundic portion of the stomach, leaving a narrow gastric tube with an intact lesser curvature connecting the esophagus and duodenum.

Deloyers and Johnson [6] investigated the secretory changes following the removal of a large amount of the fundic mucosa of dogs. They resected the greater curvature of the stomach, leaving only the cardiac region, the "air pocket," a narrow gastric tube consisting chiefly of lesser curvature and the antrum. Observations with test meals, made from the tenth to the twentieth day after operation, disclosed a definite reduction in concentration of both free and total hydrochloric acid.

Connell,[7] also working with dogs, performed a similar operation which he termed fundusectomy. Observations were made on the concentration of free acid, on the total acidity and on the emptying time of the stomach. Following the operation there was a primary delay in the emptying time, with a return to normal in about six weeks. There was also a reduction in both the concentration of free acid and the

3. Lim, R. K. S.: The Gastric Mucosa, Quart. J. Micr. Sc. **66**:187 (June) 1922.

4. Ivy, A. C., and Oyama, Y.: Secretion of the Pars Pylorica Gastri, Am. J. Physiol. **57**:51 (Aug.) 1921.

5. Mann, F. C.: Chemical and Mechanical Factors in the Experimentally Produced Peptic Ulcer, Tr. A. Am. Physicians **42**:224, 1927.

6. Deloyers, Lucien, and Johnson, J. W. S. A.: Recherches sur la topographie des régions élaboratrices de l'acide chlorhydrique dans l'estomac, Presse méd. **37**: 879 (July 6) 1929.

7. Connell, F. G.: (*a*) Fundusectomy: A New Principle in the Treatment of Gastric or Duodenal Ulcer, Surg., Gynec. & Obst. **49**:696 (Nov.) 1929; (*b*) Fundusectomy: Experimental, ibid. **53**:750 (Dec.) 1931; (*c*) Resection of the Fundus of the Stomach for Peptic Ulcer, Ann. Surg. **92**:200 (Aug.) 1932.

total acidity, with a gradual return of the latter to the normal preoperative level in about three months. The value for free acid remained low. On the basis of these results he concluded that partial fundusectomy might be of therapeutic value in the treatment of certain types of peptic ulcer.

PROCEDURE

Five dogs were used in this series of experiments. In each of the five dogs gastric and duodenal fistulas were made after the method of Mann and Bollman,[8] in order that specimens of the gastric and duodenal content could be easily and rapidly secured as frequently as desired. In each instance the duodenal fistula

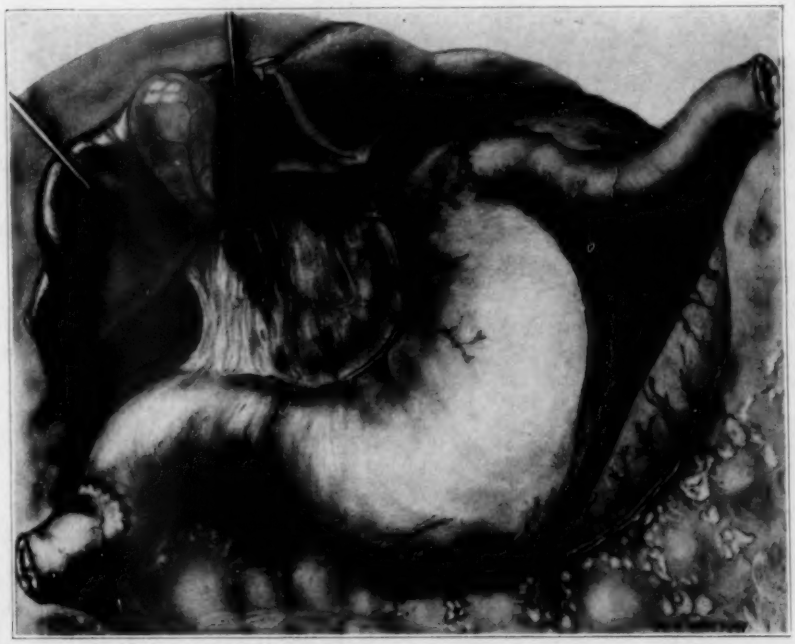

Fig. 1.—Gastric and duodenal fistulas made after the method of Mann and Bollman.

was placed on the anterior surface of the second portion of the duodenum at the level of the head of the pancreas, while the gastric fistula was placed on the anterior surface of the stomach, either in the region of the antrum or high on the cardia (fig. 1). In all surgical procedures general anesthesia and the usual surgical technic were used.

Two series of control experiments were done. The dogs were made to fast eighteen hours. Then the maximal response in gastric acidity as well as changes in the hydrogen ion concentration of the duodenal content were noted in all five animals (1) after the feeding of 100 Gm. of raw meat and (2) after subcutaneous injection

8. Mann, F. C., and Bollman, J. L.: A Method for Making a Satisfactory Fistula at Any Level of the Gastro-Intestinal Tract, Ann. Surg. **93**:794 (March) 1931.

of 1 mg. of histamine. To this end, aspirations of the gastric and duodenal content were made at fixed intervals—every hour in the experiments in which a meat meal was used and every fifteen minutes in the experiments in which histamine was used—and aspirations at these intervals were continued until the readings had returned to approximately the value during fasting. The hydrogen ion concentration of the gastric and of the duodenal content was determined by means of the quinhydrone gold electrode with a Leeds and Northrup potentiometer.[9] A sufficient amount of gastric content was aspirated each time to permit the determination of values for free acid and for total acidity; titrations were run against tenth-normal sodium hydroxide with Töpfer's reagent and phenolphthalein as indicators. Each experiment was repeated a sufficient number of times to determine the normal range of reaction and to suggest accuracy of the results.

Fig. 2.—Fundus resected after gastric and duodenal fistulas had been made.

The emptying time of the stomach of each animal also was determined with 250 cc. of a 20 per cent mixture of barium sulphate in water and observations under the fluoroscope at intervals until the stomach was empty.

After a reliable set of results had been obtained in the control experiments a second operation was performed in which most of the greater curvature of the stomach and varying amounts of the fundus, ranging from one half to four fifths of the total fundus, were resected (fig. 2). The cardia, antrum and lesser curvature were left intact. The experiments with the meat meal and with histamine were repeated from two to seven weeks and from fifteen to eighteen weeks after the operation, and the results were compared with those obtained in the control experiments. Observations on emptying time also were repeated.

9. Clark, W. M.: The Determination of Hydrogen Ions, Baltimore, Williams & Wilkins Company, 1920.

RESULTS

In analyzing the results only the maximal acid response of the stomach and the maximal effect of this response on the reaction of the duodenal content were used in each experiment. A comparison of the results obtained before removal of part of the fundus with those obtained after removal of part of the fundus should thus indicate any alteration in the ability of the stomach to respond maximally to the stimuli employed.

Gastric Hydrogen Ion Concentration.—Changes in the gastric hydrogen ion concentration following fundusectomy were at best only

TABLE 1.—*Changes in Hydrogen Ion Concentration of Gastric and Duodenal Content After Removal of Varying Amounts of Fundic Mucosa*

Stimulus	Dog	Approximate Amount of Fundus Removed	p_H		
			Control	2 to 7 Weeks After Operation	15 to 18 Weeks After Operation
			Gastric Content		
100 Gm. meat by mouth	1	1/2	1.29-1.69	1.65-1.34-1.17	1.41-1.37
	2	1/2	1.31-1.34	1.51-1.34-1.37	1.68-1.41
	3	2/3	1.24-2.54	1.63-1.46	
	4	4/5	1.32-1.33	1.32-1.49-1.51	1.32-1.46
	5	4/5	1.23-1.23	2.20-1.49	1.37-1.73
1 mg. histamine subcutaneously	1	1/2	1.07-1.33	1.22-1.17	1.40-1.40
	2	1/2	1.07-1.12	1.29-1.17	1.09-1.16
	3	2/3	1.23-1.28	1.12-1.17	
	4	4/5	1.10-1.12	1.32-1.26	1.26-1.35
	5	4/5	1.02-1.05	1.12-1.37-1.20	1.17
			Duodenal Content		
100 Gm. meat by mouth	1	1/2	4.10-4.49	4.34-4.59-3.11	4.73-4.71
	2	1/2	4.04-4.92	4.81-5.18-4.44	5.06-3.78
	3	2/3	4.04-5.24	6.00-5.18	
	4	4/5	3.62-3.39	4.15-3.15-4.12	3.09-3.78
	5	4/5	4.23-4.42	3.10-5.67	
1 mg. histamine subcutaneously	1	1/2	2.90-5.98	5.98-5.41	6.57-4.66
	2	1/2	5.47-6.49	5.93-5.41	1.80-6.12
	3	2/3	6.07-7.38	7.12-7.27	
	4	4/5	1.39-5.24	5.17-5.29	2.10-2.26
	5	4/5	4.50-6.39	5.46-6.48-6.63	

slight in most of the experiments and were consistently seen in only two dogs, from which approximately four fifths of the fundus had been removed (table 1).

Duodenal Hydrogen Ion Concentration.—The duodenal hydrogen ion concentration was only slightly affected by fundusectomy, and the changes that did occur were inconstant. Alterations occurred more frequently after the meat meal and were rarely seen after the administration of histamine (table 1).

Free Acid.—The concentration of free acid in the gastric content of one animal (dog 3) was not changed following fundusectomy when either meat or histamine was given. Two animals (dogs 1 and 2) sometimes gave evidence of a reduction of free acidity of the gastric content after histamine had been given and sometimes after meat had

been given; reduction was not an invariable occurrence nor was it consistent. Free acidity of the gastric content of the two remaining of the five animals (dogs 4 and 5) was reduced in almost all instances after the administration of either meat or histamine. From both of these two animals approximately four fifths of the fundus had been removed. Late observations on these last animals in most instances disclosed less marked reduction in the value for free acid than had been obtained from two to seven weeks after fundusectomy (table 2).

Total Acidity.—Total acidity of the gastric content of one dog (dog 3) was not changed after fundusectomy following the meat meal

TABLE 2.—*Maximal Response in Concentration of Free Acid and in Total Acidity of the Gastric Content* *

Stimulus	Dog	Approximate Amount of Fundus Removed	Control	2 to 7 Weeks After Operation	15 to 18 Weeks After Operation
			Free Acid		
100 Gm. meat	1	1/2	40.0-75.0	35.0-60.0-90.0	70.0-70.0
	2	1/2	65.0-85.0	50.0-60.0-60.0	42.5-65.0
	3	2/3	45.0-60.0	45.0-45.0	
	4	4/5	75.0-77.5	72.5-50.0-52.5	70.0-92.5
	5	4/5	90.0-90.0	10.0-55.0	70.0-37.5
1 mg. histamine	1	1/2	128.0-140.0	85.0-90.0	70.0-92.5
	2	1/2	121.0-123.0	70.0-96.0	124.0-108.0
	3	2/3	87.0-111.0	110.0-88.0	
	4	4/5	108.0-115.0	68.0-71.0	80.0-72.0
	5	4/5	116.0-129.0	100.0-65.0-92.0	90.0
			Total Acidity		
100 Gm. meat	1	1/2	120.0-140.0	100.0-130.0-137.5	142.5-160.0
	2	1/2	125.0-140.0	110.0-120.0-120.0	132.5-195.0
	3	2/3	155.0-170.0	170.0-185.0	
	4	4/5	145.0-155.0	95.0-115.0-127.0	125.0-162.5
	5	4/5	160.0-165.0	80.0-120.0	135.0-140.0
1 mg. histamine	1	1/2	138.0-150.0	102.5-104.0	105.0-122.5
	2	1/2	131.0-133.0	85.0-108.0	166.0-142.0
	3	2/3	100.0-125.0	124.0-106.0	
	4	4/5	120.0-125.0	86.0- 93.0	103.0-102.0
	5	4/5	128.0-141.0	114.0- 75.0-108.0	110.0

* Estimated by Töpfer's method.

or after the administration of histamine; another (dog 1) gave no evidence of change after the injection of meat but showed a definite reduction after the administration of histamine, while a third (dog 2) gave evidence of definite reduction in the early observations after the ingestion of meat and after the administration of histamine, but later normal values returned irrespective of whether meat or histamine had been given. The two dogs from which approximately four fifths of the fundus had been removed continued to give evidence of some reduction in total acidity throughout the whole series of observations, although the reduction in the value for total acid in most instances was not so marked in the late observations (table 2).

Relation Between the Amount of Fundus Removed and the Effect on Gastric Acidity.—It is evident that there is some correlation between the

amount of fundus removed and the subsequent effect on gastric acidity, for only in the two dogs from which approximately four fifths of the fundus had been removed were alterations consistently found in the gastric hydrogen ion concentration, concentration of free acid and total acidity, while in the three dogs from which smaller amounts had been removed there were slight or only occasional changes. No such correlation could be detected, however, in the group in which smaller amounts of fundic mucosa were removed. Thus, one dog, from which approximately two thirds of the fundus had been removed, gave no evidence of changes in the gastric hydrogen ion concentration, free acid or total acidity, while the other two, from which tissue estimated to represent approximately one half of the fundus had been removed, gave evidence of occasional changes. Failure to find any correlation here possibly results from the difficulty of accurately estimating the amount of tissue removed. That there was a difference between the amount of fundus removed from the dogs which consistently gave evidence of change and the amount removed from those which gave no evidence of change or of only occasional change is certain, for from the former as much of the fundus was removed as was possible, while in the latter fundic tissue that could have been removed was allowed to remain.

Emptying Time.—Fluoroscopic examination of the stomach of the dogs in the control observations disclosed that the emptying time varied between one hour and twenty minutes and two hours. Following fundusectomy there was acceleration of the emptying time of the stomach in most of the dogs, with a gradual return to normal in from fifteen to eighteen weeks. In two of the dogs there was a slight delay in emptying of the stomach.

COMMENT

Although the results of any study of gastric acidity are likely to be open to question because of the wide variations that can occur, the usual objections seem scarcely valid if only the maximal response to a definite stimulus is used. The use of two different types of stimuli was resorted to, more with the idea of having two different sets of results to check against each other than because of any special merits of the one over the other.

The results obtained in these experiments appear to confirm most of the work of other investigators. The experimental ulcers obtained by Mann and Bollman [8] when fundusectomy was performed at the same time as, or preceding, surgical duodenal drainage indicate that the increased degree of chronicity which these authors noted was the result of reduction in the amount of acid produced in the stomach, even though this was not sufficient entirely to prevent the formation or

development of the ulcers. The results of Deloyers and Johnson [6] and those of Connell [7b] as well as mine clearly show that there is a reduction in both the concentration of free acid and in total acidity immediately following operation, when most of the fundic mucosa has been removed.

Connell,[7b] in his observations which extended over a period of three months, found that the concentration of free acid remained reduced but that total acidity returned to normal. I found this phenomenon in only one dog from which approximately one half of the fundus had been removed, and even with this animal the result was obtained only in experiments with the meat meal; following the administration of histamine values for both free acid and total acidity were normal in the later observations. In the gastric content of dogs from which approximately four fifths of the fundic mucosa was removed there was persistent reduction of both the concentration of free acid and the total acidity throughout the whole course of the experiment, although reduction of either total or free acidity was usually not as marked in the late as in the early observations. In most instances the differences between early and late results were roughly the same both for the concentration of free acid and for the total acidity, and any alteration in the one was reflected in the other.

This reduction in the acidity of the gastric content undoubtedly results from the quantitative diminution in the secretion of acid brought about by the removal of a large portion of the acid-secreting fundus. Attempts to prove such quantitative changes were made in the histamine tests, and at each aspiration an effort was made to withdraw and measure all the secretion present in the stomach. Although I could never be certain that I had aspirated all the secretion present, the amount obtained at the height of the reaction after fundusectomy was definitely less than the amount secured before fundusectomy. As a rule the reduction in concentration of free acid was more marked than the reduction in total acidity. This would indicate that after fundusectomy the gastric content has relatively an increased amount of acid existing in the combined form and that this may result from alteration in the ratio of the amount of mucus and acid secreted, for the antrum and cardia remain untouched by the operation, and thus the amount of mucus secreted should remain unchanged.

Failure of gastric acidity to change at all or more than occasionally after resection of approximately one half to two thirds of the fundic mucosa and its failure to change more than moderately after the removal of a still greater amount attest to the fact that the stomach possesses that same wide factor of safety that is possessed by so many other organs of the body, permitting it to act almost normally even after extensive resection of its acid-secreting tissue. The value of such a procedure in

surgical treatment of those conditions of man which demand reduction in gastric acidity can be properly determined only by its direct application.

SUMMARY

The changes in gastric acidity were studied before and after resection of varying amounts of fundic mucosa. Alterations in gastric acidity as determined by changes in the hydrogen ion concentration were very slight, while alterations in the hydrogen ion concentration of duodenal content were rarely seen. Definite reductions in both concentration of free acid and total acidity were noted immediately after operation in those dogs in which extensive resection was performed, but in subsequent observations at the end of four months the changes were less marked.

WOUND HEALING AFTER ANTERIOR GASTRO-ENTEROSTOMY

II. FATE OF MUCOSAL INCLUSIONS AND THEIR PREVENTION; DESCRIPTION OF A NEW SUTURE TECHNIC. AN EXPERIMENTAL STUDY IN DOGS

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AND

GEORGE R. SUCKOW, M.D.

PORTLAND, ORE.

In a previous experimental study [1] we attempted to reproduce serosal inclusions such as are found at times on the female parietal and visceral peritoneum and showed that when two serosal surfaces are brought together as in a gastro-enterostomy no recognizable serosal inclusions (celomic epithelium) are formed. This result was not unexpected in view of the studies of Ranvier and Marchand,[2] Cunningham,[3] Foot [4] and others. However, we believed it possible that such inclusions might have been overlooked when an investigator was engrossed in some other phase of the problem of the behavior of celomic epithelium. As noted, our search in this respect was fruitless.

On the other hand, we did find that when we employed suture methods on the anterior aspect of gastro-intestinal anastomoses that everted mucosa into the line of apposition between stomach and intestine, then mucosal inclusions (appositional rests or inclusions) similar to

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From the Departments of Surgery and Physiology, University of Oregon Medical School.

This work was aided in part by Grant no. 178 from the Committee on Scientific Research, American Medical Association, by a grant to the medical school by the General Education Board.

Our experiments and observations were completed in January 1931, and the substance of this paper was reported at a meeting of the North Pacific Surgical Society, Dec. 3, 1931. Illness has prevented prior publication.

1. Martzloff, K. H., and Suckow, G. R.: Wound Healing in Anterior Gastro-Enterostomy Following Various Methods of Suture: An Experimental Study in Dogs, Arch. Surg. **26**:345 (March) 1933.

2. Ranvier and Marchand, quoted by Cunningham.[3]

3. Cunningham, R. S.: The Changes in the Omentum of the Rabbit During Mild Irritations, with Special Reference to the Specificity of the Mesothelium, Bull. Johns Hopkins Hosp. **33**:257, 1922.

4. Foot, N. C.: Studies on Endothelial Reactions: V. The Endothelium in the Healing of Aseptic Wounds in the Omentum of Rabbits, J. Exper. Med. **34**:625, 1921.

those shown in figures 2, 3 and 4 occurred between their walls and were observable for as long as twenty days after operation. This was particularly noticeable when the innermost suture on the anterior aspect of the anastomosis was a continuous, through-and-through circular stitch (technic 5) which is commonly recommended in surgical textbooks [1] (fig. 1).

Another type of mucosal inclusion was observed to occur about silk serosubmucosal sutures when they pierced the intestinal mucosa. These we termed "suture inclusions" in contradistinction to the aforementioned appositional inclusions.

We also observed that most rapid and uncomplicated healing from mucosa to serosa on the anterior aspect of a gastro-intestinal anastomosis

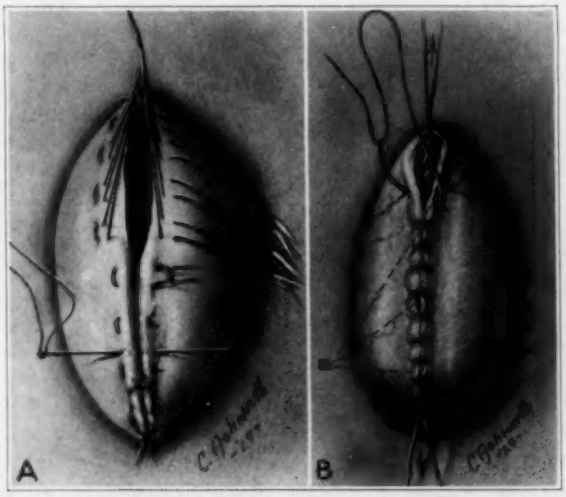

Fig. 1.—*A* is a demonstration of suture method 4, the Halsted presection suture technic, used only on the anterior aspect of the ostium. *B* is a demonstration of suture method 5, the ordinary continuous circular through-and-through suture which when used anteriorly inevitably causes macroscopic mucosal eversion as shown at *a* (Martzloff and Suckow [1]).

occurred with the Halsted presection suture method, which for the sake of brevity we have referred to as technic 4. With this method the sutures are in the serosubmucosa (fig. 1), and the mucosa therefore is neither sewed nor everted. All these observations were made and confirmed on two separate series of dogs.

In this study which was begun after our first two series had been completed we have had as our purpose three principal objects: (1) to repeat, on a third and separate series of animals, the finding of mucosal inclusions in the anterior line of apposition of gastro-intestinal anastomoses after the use of the ordinary through-and-through circular con-

tinuous suture (technic 5); (2) to study the fate of these appositional inclusions after a longer period of healing (ninety days), and (3) to develop a practical two layer suture method that would permit approximately the rapid healing obtained by the one layer Halsted presection suture method and at the same time eliminate some of the objectionable features of the other multilayer suture methods that are generally used on the anterior aspects of gastro-enterostomy ostia.

The present study was carried out on twenty-two dogs. Two of these died of bronchopneumonia (autopsy) on the third postoperative day during an epidemic of "snuffles," leaving twenty animals available for the observations reported here.

TECHNIC AND OBSERVATIONS ON RESULTS

In five dogs (nos. 54, 59, 60, 63 and 72) suture technic 5 was used, and healing was studied nine, fourteen, twenty, thirty-one and thirty-four days after operation. In view of the protocols given in our previous study we omit them here, because this series substantiates our earlier observations on the effect of this suture method on the anterior aspect of gastro-intestinal anastomoses. Briefly, appositional mucosal inclusions were well developed in one animal (no. 60) twenty days after operation, and some small deeply placed glands were found in the line of apposition nine days after operation in dog 72. In the latter animal there was also a well defined defect with a pyogenic membrane on the mucosal aspect of the apposed stomach and intestine where mucosal regeneration had not occurred. In dog 59, after fourteen days we could not be certain whether a well developed mucosal inclusion was appositional or a suture inclusion.

In three animals (nos. 54, 60 and 63) well marked silk suture defects lined by intestinal mucosa (suture inclusions) were encountered in the wall of the intestine. In a fourth animal (no. 59), previously noted, the origin of a mucosal inclusion was debatable.

In other words, the observations in our first report have been confirmed: Suture technics, particularly the continuous through-and-through circular suture (method 5), by which gastro-intestinal mucosa is everted, cause mucosal inclusions in the line of apposition in an appreciable proportion of experimental animals. The question of mucosal inclusions caused by silk suture is another matter and, as we have pointed out, depends on the nicety and precision with which silk sutures are placed. This in turn is in part dependent on the degree of distortion the preceding suture has given to the line of anastomosis. In the entire present series of twenty animals, when silk suture inclusions occurred they were on the intestinal side of the anastomosis.

Fate of Mucosal Inclusions.—In order to see whether the mucosal inclusions we had observed in the anterior aspect of gastro-intestinal anastomoses actually persist, eight dogs (nos. 53, 55, 56, 57, 58, 66, 69 and 73) were operated on and killed after a period of from ninety to ninety-seven days. In each instance an innermost continuous circular through-and-through suture of plain 00 catgut (technic 5) was used on the anterior aspect of the gastro-intestinal anastomosis, followed by a second row of interrupted mattress sutures (Halsted's) of 0 black silk. This was identical with technic 5 used in each of our previous experimental series.

Large mucosal inclusions in the line of apposition (appositional inclusions) were observed in four animals (nos. 53, 56, 57 and 73). Serial sections were made and studied in three of the animals killed after ninety days (nos. 53, 56 and 57) and in three other animals (nos. 45, 49 and 54) belonging to an earlier series. Observations made on the latter after healing periods of fourteen, twenty and thirty-four days, respectively, following the same suture technic (method 5) were included in our first report. However, serial sections were not available at that time. Our protocols covering observations on the animals killed after ninety days are given here in briefest outline.

Dog 53 (ninety-day healing period).—Mucosal healing was complete with the formation of glands up to the point where the two layers of mucosae (gastric and intestinal) unite. The point of transition was abrupt, and gastric parietal cells extended up to and stopped abruptly where the mucus-secreting cells of the intestinal mucosa began. The muscularis of the stomach and that of the intestine were united by, and frayed out into, a broad zone of connective tissue. There was a well defined mucosal inclusion in the line of apposition. This had a glandular structure and membrana propria characteristic of intestinal mucosa. There was no definite celluar infiltration about this inclusion. Farther out toward the serosa was a definite though moderate infiltration of round and polymorphonuclear cells. The mucosal inclusion in serial section finally effected a free communication with the gastro-intestinal lumen. In its deepest ramification (slide 5) the mucosa of the inclusion minus the muscularis mucosae penetrated almost the entire thickness of the circular muscularis and lay within 1 mm. of the serosa as an excessively deep gastro-intestinal crypt, in the depths of which gastric and intestinal mucosa meet.

Dog 55 (ninety-day healing period).—Mucosal healing was complete, as in dog 53. Mucosal marginal cysts were seen on the intestinal side of the line of mucosal apposition. The muscular layers of the stomach and intestine were united by a narrow zone of connective tissue. A silk suture in the intestinal wall was immediately surrounded by monocytes and recognizable fibroblasts. In one place a multinuclear giant cell occurred, while only an occasional lymphocyte or polymorphonuclear leukocyte was seen. A dense fibrous stroma in turn surrounded all this. No mucosal inclusions were seen. We would consider this a good end-result.

Dog 56 (ninety-day healing period).—Sections showed excellent restitution at the point of gastro-intestinal mucosal apposition. However, farther out in the line of apposition was a large bilocular mucosal inclusion lined by a flattened layer of epithelium (fig. 2). External (toward the serosa) to this was another mucosal inclusion lined by intestinal epithelium containing a silk thread and some exudate and communicating with the intestinal lumen at a point about 1 cm. distant from the point of gastro-intestinal mucosal apposition. There was a moderate infiltration of round and polymorphonuclear cells about this suture inclusion which had the appearance of an interstitial diverticulum. Where this inclusion communicated with the intestine there were a marked loss of intestinal mucosa and a marked eosinophilic infiltration into the remains of the basement membrane. There was not, however, sufficient histologic evidence to warrant the conclusion that this mucosal loss was entirely due to ulceration. More likely it represented, in part at least, a technical artefact due to sectioning. In serial sections this inclusion showed considerable change in form, but no distention. The appositional inclusion first mentioned in serial section showed other septums crossing its lumen so that it was multilocular. At no time did it communicate with the gastro-intestinal lumen.

Dog 57 (ninety-day healing period).—Mucosal healing was excellent. A glandular mucosal inclusion surrounded by compact fibrous stroma was seen right in the line of apposition within 1 mm. of the serosa. The adjacent subserosa showed moderate infiltration by round and polymorphonuclear cells. On the gastric side of the line of apposition was a mucosal inclusion with a surrounding leukocytic infiltration which resembled a suture inclusion, but no silk was seen. However, the presence of large monocytic cells and large spindle-shaped cells (fibroblasts)

Fig. 2 (dog 56, method 5, ninety day healing period).—This shows two types of mucosal inclusions. At *b* is an appositional mucosal inclusion which is bilocular, distended and lined by a smooth layer of flattened epithelium. In serial sections this inclusion shows other septums, remains distended and does not communicate with the gastro-intestinal lumen. At *c* is a mucosal inclusion lined by a single layer of mucosa and associated with a silk suture (suture inclusion). It contains exudate, is surrounded by inflammatory reaction and communicates with the intestinal lumen (*I*) where there is a large mucosal defect that is explained in the text. *S* indicates the wall of the stomach. Gastric and intestinal mucosa meet at *a*.

was typical of the reaction ordinarily seen about silk. This inclusion appeared to come from the gastric mucosa since the muscularis mucosae at this point showed an interruption with a few typical gastric glands lying in the submucosa but not in communication with the inclusion. This inclusion represented the only probable

suture inclusion we had seen involving the stomach, and we were unable to find it in our serial sections.

Serial sections, however, did show the aforementioned appositional inclusion in brief communication with the gastro-intestinal lumen. The inclusion (fig. 3) possessed a complex glandular structure resembling intestinal mucosa, and the gastro-intestinal mucosa overlying it showed marked loss of substance and a well defined inflammatory reaction. In serial sections from another block another set of appositional inclusions were seen (fig. 4). These contained exudate and had an obliquely burrowing, tortuous communication, 0.5 cm. long, with the gastro-intestinal lumen at the point of union with the gastro-intestinal mucosa. This communication was again lost, so that the ultimate result was a mucosal sinus

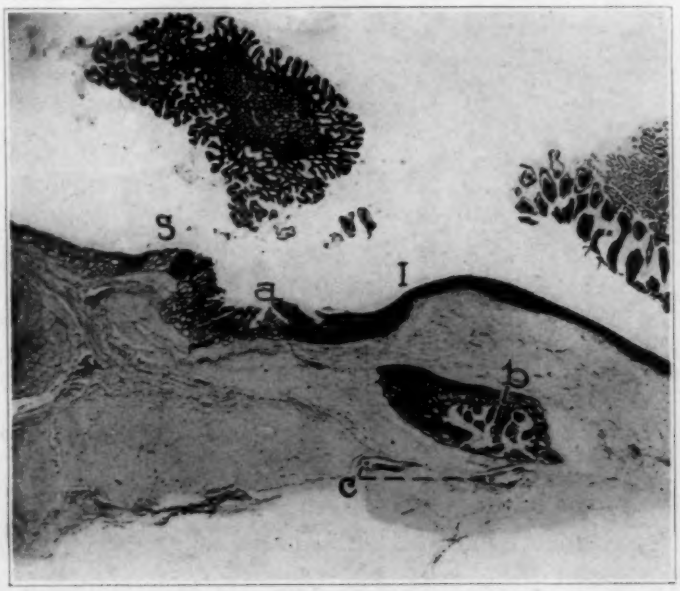

Fig. 3 (dog 57, method 5, ninety day healing period).—*a* is the point where the gastric and intestinal mucosa meet; *b* is a glandular appositional mucosal inclusion between the wall of the stomach (*S*) and that of the intestine (*I*) with a surrounding inflammatory reaction. The mucosa of the stomach and of the intestine show loss of substance and inflammatory reaction (other sections show this inclusion communicating with the gastro-intestinal lumen). Silk sutures in the wall escaping into the peritoneal cavity are indicated by *c*.

which extended in two directions from a central communication with the gastro-intestinal lumen. No recognizable gastric mucosa was seen in the inclusion. The deeper portion of the inclusion maintained a position close to the serosa. A large marginal cyst on the gastric side of the line of apposition remained intact and did not communicate with the gastro-intestinal lumen.

Dog 58 (ninety-day healing period).—Healing at the point of gastro-intestinal mucosal apposition was abnormal as compared with the other animals examined after ninety days. The mucosa was shallow and devoid of glands; some exudate was seen in the lumen, and there was an infiltration of the neighboring papillae

by polymorphonuclear cells. There was also an infiltration by round and polymorphonuclear cells extending from the mucosa into the connective tissue that united the walls of the stomach and the intestine. All this was due to a silk suture in the muscularis of the intestine which had worked its way into the gastro-intestinal lumen at the line of apposition. No mucosal inclusions were seen.

Dog 66 (ninety-four day healing period).—Observations on the sections were irrelevant except for some marginal cysts in the gastric mucosa and a long, narrow mucosal inclusion in the muscularis of the intestine well to one side of the line of apposition. Because of its position we recognized this as a suture inclusion, although no silk was seen associated with it. The line of gastro-intestinal apposition showed a moderate amount of scar tissue. Two silk sutures in this area showed a moderate infiltration by round and polymorphonuclear cells in addition

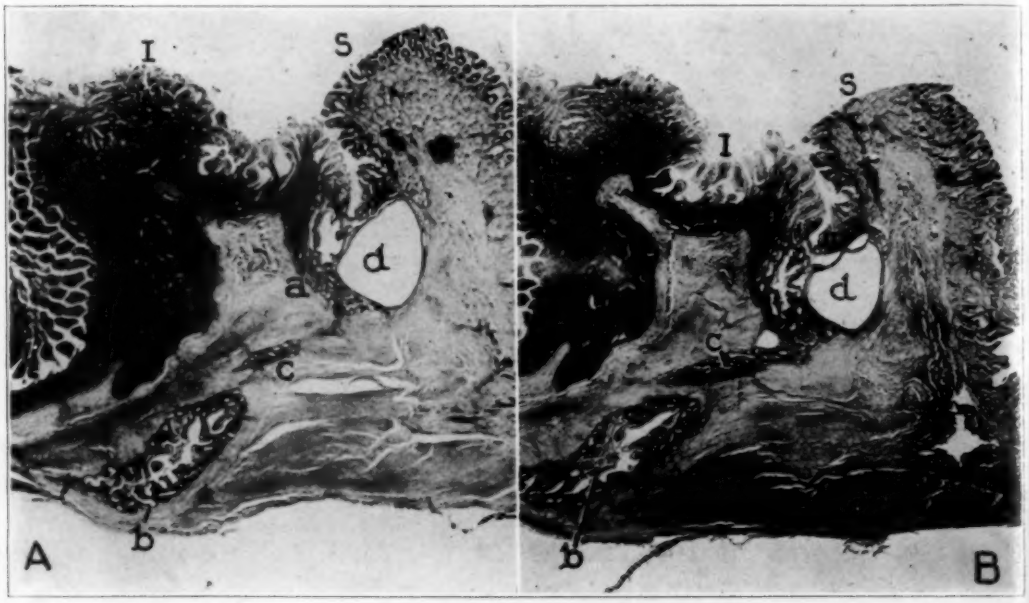

Fig. 4 (dog 57).—In *A* the glanduar appositional inclusion at *b* is not a continuation of the one shown in figure 3. At *c* another glandular inclusion is seen. A large marginal cyst is seen at *d* which does not communicate with the gastro-intestinal lumen. In *B* the appositional inclusion (*c*) communicates with the gastro-intestinal lumen. Sections farther along in the block showed inclusion *b* joining with *c* and so communicating with the gastro-intestinal lumen. *I* and *S* indicate intestine and stomach, respectively.

to the customary large monocytic cells that immediately surrounded the fragmented silk. There was also moderate infiltration of the subserosa by round and polymorphonuclear cells.

Dog 69 (ninety-day healing period).—Observations on the sections were essentially irrelevant except for some silk suture defects near the line of apposition which contained exudate and an infiltration by surrounding round and polymorphonuclear cells. On the basis of previous experience it is a fair assumption that this suture communicated with the gastro-intestinal lumen at some point, although the

sections did not show it and serial sections were not made. There was a moderate infiltration into the subserosa by round cells.

Dog 73 (ninety-seven day healing period).—Observations on the sections were irrelevant except for a mucosal inclusion in the line of apposition. This measured 0.5 cm. in diameter and had a basement membrane and intestinal villi in places, some of the villi showing aggregations of polymorphonuclear leukocytes. The inclusion extended to within 1.5 mm. of the serosa, and there was a definite though moderate cellular infiltration containing some plasma cells in the subserosa. A marginal cyst was seen right in the line of gastric and intestinal mucosal apposition.

Dogs 45, 49 and 54 (fourteen, twenty and thirty-four day healing periods).—Observations on serial sections merely confirmed our previous observations. In dog 45 a glandular inclusion in the line of anastomosis (appositional inclusion)

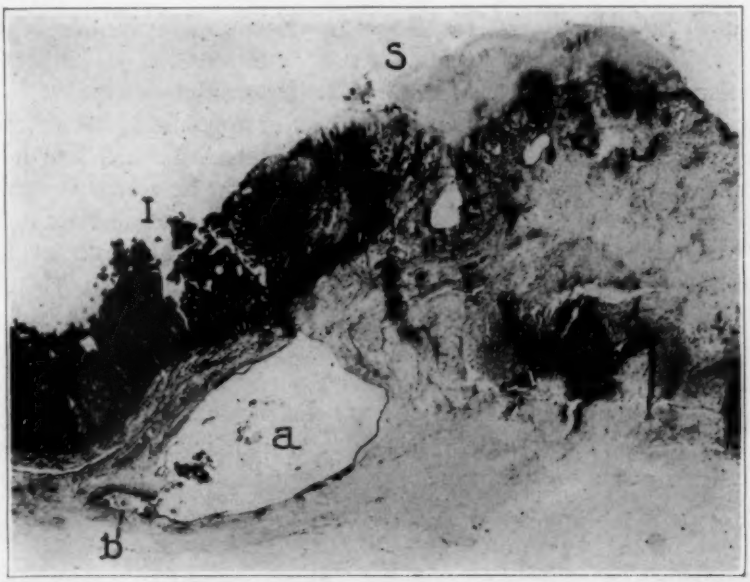

Fig. 5 (dog 54, method 5, thirty-four day healing period).—This section shows a cystic suture (?) inclusion (*a*) which is distended and in serial section shows no communication with the gastro-intestinal lumen. The inclusion contained silk, exudate and a low columnar epithelial lining membrane. There was an inflammatory reaction about the inclusion. A sinus (*b*) lined by granulation tissue and a pyogenic membrane communicated with the cystic structure (*a*). *S* indicates necrotic gastric mucosa and *I*, intestinal mucosa.

did not develop a communication with the gastro-intestinal lumen. This inclusion was not seen in the sections studied for our first report but came to light after the block was cut into for the purpose of tracing a suture inclusion. In dog 49 the appositional inclusion reported in our first paper was found to have developed a communication with the gastro-intestinal lumen and to disappear, being replaced by an area of marked inflammatory reaction. A suture inclusion in the wall of the intestine showed no opening into the intestine although it was involved in a pronounced inflammatory process, and the suture, judging from the course of the

inflammatory reaction, was discharging into the peritoneal cavity. However, we did not actually demonstrate this. In dog 54 the large mucosal inclusion about a silk suture in the intestinal wall, reported in our first paper, remained distended and contained exudate and in serial section was not found to communicate with the intestinal lumen (fig. 5). In fact, this inclusion apparently occurred right in the line of apposition. Whether it was primarily an appositional inclusion or a suture inclusion one cannot say, for it is possible that the silk suture was incorporated in an appositional inclusion.

COMMENT

The results obtained on this series of animals confirm our previous observation that suture methods which tend to evert the mucosa into the line of apposition in gastro-intestinal anastomoses cause mucosal inclusions in an appreciable number of animals (50 per cent in this series). These inclusions persist, for they were found ninety days after operation, and when they do not establish a communication with the gastro-intestinal lumen they may form cysts of appreciable size. When, however, an inclusion does open into the gastro-intestinal lumen the communication in our specimens has been narrow in comparison with the size of the inclusion, and dilatation of the inclusion did not occur. In some specimens these inclusions were accompanied by inflammatory phenomena after a ninety day period of healing. This we judge to be definitely pathologic when we consider that anastomoses performed by suture methods which are not complicated by mucosal eversion show an almost complete absence of inflammatory phenomena after a healing period of twenty days or less. Appositional mucosal inclusions, therefore, are undesirable complications even though our observations did not indicate any more untoward effects than those we have described.

SUTURE METHODS

Connell's and Halsted's Method.—The suture methods with which we obtained no appositional mucosal inclusions in our previous study were the Connell suture and the Halsted presection suture method. The former is a two layer suture method in which the first suture layer along the anterior aspect of the gastro-intestinal ostium is a through-and-through continuous right-angled catgut stitch that does not cross the free mucosal margins. As far as our experimental observations are concerned the suture is practical and satisfactory, although it is associated with considerable inflammation and delayed mucosal healing as compared with the Halsted method. However, with the exception of the latter we consider it superior to any of the multilayer suture methods from the standpoint of its practical application and ultimate healing. The Halsted presection method is a one layer suture method used on the anterior aspect of the gastro-intestinal anastomosis which avoids suture eversion or purposeful penetration of the mucosa.

In this method a number of Halsted's serosubmucosal mattress sutures of 0 black silk are loosely placed before the stomach and intestine are opened. These presection sutures are retracted, the stomach and intestine are incised and a suture of catgut (second posterior layer) is placed through all thicknesses of the stomach and intestine for hemostasis on the posterior aspect of the ostium. Bleeding points on the anterior aspect of the ostium are ligated individually. The presection sutures are now drawn up and tied and any additional sutures are placed where needed. This, as we previously reported, results in perfect infolding of the gastro-intestinal mucosa and serosa, absence of mucosal inclusions in the line of apposition, and a rapidity of healing that surpasses that of any of the other methods used. A practical disadvantage which this method has is that it may become very bunglesome if the operating team is not familiar with its technic, while a two layer suture technic avoids this fault. For this reason and because many surgeons depend on at least one suture-line for hemostasis along the anterior aspect of the ostium methods calling for two and sometimes three layers of sutures are commonly employed.

Three Layer Suture Method.—On the basis of our reported experimental observations [1] we can see no advantage to a three layer suture technic which has the disadvantage of an additional technical step and the excessive use of suture material. The separate suturing of the mucosa (mucosa and submucosa) which a three layer technic ordinarily employs does not in our experience hasten mucosal union but is rather a retarding factor when compared with methods which do not require suturing of the mucosa.

Anterior Method 7 (Two Layer Serosubmucosal Suture).—In order to have a simple and practical two layer suture method for the anterior aspect of a gastro-intestinal anastomosis which would avoid eversion of the mucosa with consequent formation of appositional mucosal inclusions and suture trauma to the mucosal margins and at the same time provide hemostasis to control capillary oozing (not important bleeding points, which should be ligated) and would permit rapid and uncomplicated healing comparable to that obtained with the Halsted presection method, we employed a suture method we have not heretofore seen described. This method we believe fulfils the requirements we have mentioned, and we have referred to it in our protocols as anterior method 7. It is actually a two layer serosubmucosal suture.

The catgut suture (00 plain) which has been used posteriorly as the innermost layer is continued anteriorly as the innermost anterior layer to unite the stomach and the intestine. The suture is carried on a fine, curved or straight intestinal needle which is always directed obliquely toward the cut edge of the stomach or intestine and in the

direction of the unsutured defect, as shown in figure 6. The needle is inserted about 0.5 cm. from the cut edge of the viscus. It should penetrate only as deeply as the outermost layers of the submucosa and should come out at the cut edge of the viscus so as to pierce the muscularis and avoid the cut edge of the mucosa. The latter point may sound like a highly theoretical and unpractical refinement. As a matter of fact, it is a relatively simple and practical procedure, as we have found experimentally and on patients.

However, the first proposition, i. e., placing this suture only as deep as the outermost layers of the submucosa, is open to technical criticism. Obviously insertion of intestinal sutures with a curved needle on a needle holder makes accurate placement in the outer layers of the sub-

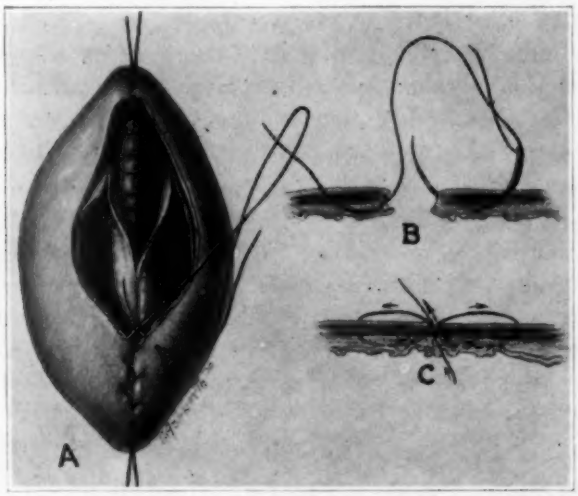

Fig. 6.—A demonstration of our two layer serosubmucosal suture (anterior method 7) with an ordinary serosubmucosal suture (*A*) used posteriorly while the mucosa is not sutured. Normally the mucosal edges fall together. This procedure we consider relatively impracticable, as described in the text. Anteriorly the suture we have described is shown. *B* and *C* are self explanatory and illustrate in cross-section the suture which permits healing that is almost as uncomplicated and rapid as that which follows the single layer Halsted presection technic (method 4). The anterior suture layer in *A* is drawn up more closely than is illustrated in *A* and *C* so as to cause serosal inversion. This is then reinforced by a layer of Halsted's mattress sutures which are not ilustrated.

mucosa impossible. Therefore, penetration of the mucosa, particularly on the thin-walled intestinal side, is a relatively common though not serious fault when catgut is used. When the suture is tensed it brings the cut edges of the stomach and intestine together as shown in figure 6 *c*. Further tension inverts the serosa, and further inversion is effected by a second row of Halsted's silk mattress sutures which

complete the anastomosis. Care is taken during this procedure to avoid instrumental trauma to the mucosa. The edges of the cut viscera are therefore manipulated by grasping the seromuscular layer with fine mouse-tooth forceps. Everting mucosa is readily inverted by an assistant with any suitable instrument with a smooth surface.

We cannot understand the rationale of resecting the so-called redundant mucosa, for it apparently plays a rôle in covering the surgical defect, and its resection would apparently create defects greater than those we have demonstrated in our previous report. However, we have produced no direct evidence to support this assumption. Five animals (nos. 70, 71, 74, 75 and 76) were employed for gastro-intestinal anastomosis in which our two layer serosubmucosal inverting suture (anterior method 7) was used on the anterior aspect of the ostium. One animal died of pneumonia on the second postoperative day (day after operation) and this specimen was not studied.

After six days, counting the day of operation as the first postoperative day, specimens (dog 74) showed that the line of mucosal apposition was nowhere actually devoid of mucosa. However, the gastric mucosa, while present at and near the line of apposition, was low and definitely damaged, showing a moderate infiltration by polymorphonuclear cells and some overlying exudate. Except at the point of apposition the mucosa lay on a recognizable muscularis mucosae. Right at the point of gastro-intestinal mucosal apposition new gastric mucosal cells joined the relatively undisturbed intestinal epithelium. Farther away (from 1 to 2 mm.) from the point of apposition on the gastric side was a small defect about 2 mm. long which was devoid of a covering epithelium, but scattered through this small zone which contained granulation tissue were viable mucosal cells. The intestinal mucosa near the line of apposition also showed some loss of substance which was limited to the superficial layers. Proceeding out toward the serosa along the line of apposition rather compact young fibrous stroma was seen. This was almost devoid of cellular infiltration except where the remains of a catgut suture was associated with a dense polymorphonuclear exudate. Farther out near the serosa the intestinal wall contained a silk suture defect with a glandular mucosal suture inclusion and an associated intense inflammatory reaction.

Specimens from dog 76 showed better mucosal healing than those from dog 74. Gastric and intestinal mucosa showed a glandular structure and only a superficial disturbance (figs. 7 and 8). At the point of mucosal apposition was an area, a fraction of a millimeter in length, devoid of epithelium. The muscularis mucosae on both sides extended up to the point of apposition. On the intestinal side about 2 mm. from the point of mucosal apposition the muscularis mucosae and mucosa showed an abrupt interruption for about 1 mm. Here the overlying

mucosa was lost, and the remaining portion showed distortion and cellular infiltration which extended into the superficial portion of the submucosa. We believe that this indicates an area where the catgut suture was passed too deeply. Farther out in the line of apposition

Fig. 7 (dog 76, anterior method 7, six day healing period).—The point of gastric (*s*) and intestinal (*I*) mucosal apposition is shown at *a* where there is a small area devoid of epithelium and a small long plug of exudate at *b*. *X* indicates a small area devoid of intestinal mucosa composed of a hyaline-appearing zone with some cellular infiltration lying on the muscularis mucosae. Silk threads are indicated at *c* near the serosa. The photomicrograph has been retouched to bring out the boundaries between the gastric and intestinal mucosa and their underlying submucosa.

between the stomach and the intestine excellent healing had occurred, with less cellular infiltration than in dog 74. The silk sutures in these sections showed almost total absence of surrounding inflammatory phenomena.

A nine day specimen (dog 70) showed remarkable mucosal union. The mucosa was of about normal thickness and had a glandular structure which, however, showed distinct alteration (figs. 10 and 11). The muscularis mucosae of the stomach and intestine was intact up to the point of mucosal apposition. Farther out in the line of apposition between the stomach and intestine was compact fibrous union with little

Fig. 8.—A higher magnification of the area of mucosal apposition shown in figure 7. At *a* is the small area devoid of epithelium at a point of gastric and intestinal mucosal apposition. *I* indicates intestine, *s*, stomach, and *b* a plug of exudate.

cellular infiltration except around some silk sutures which were associated with an intense cellular infiltration and a mucosal inclusion on the intestinal side.

Results after a healing period of fourteen days (dog 71) were merely an improvement on those in dog 70. Union along the line of apposition was compact and without cellular infiltration except around the broken up, hyaline-appearing remains of a catgut suture which was associated with a moderate infiltration by round cells. No silk was seen.

The healing, both mucosal and interstitial, following the use of our serosubmucosal two layer inverting suture (method 7) on the anterior aspect of the gastro-intestinal anastomosis surpasses that obtained by any other method we have used except the one layer Halsted presection method (method 4). In addition, the method eliminates the undesirable appositional mucosal inclusions and lends additional support to our observation that suture of the mucosa is not only superfluous but undoubtedly complicates and retards rapid healing.

Fig. 9 (dog 21, method 4 [Halsted's presection method] six day healing period). —This section is shown to compare with figure 7. At *a* is a point of gastric (*S*) and intestinal (*I*) mucosal union completely covered by epithelium. *X* indicates two lymph follicle-like aggregations of round cells. Healing in the line of apposition from the mucosa to the serosa was excellent.

Posterior Suture Methods.—These were discussed in our previous paper and observations on this series add no further information. We should state that an adaptation of anterior method 7 to the innermost posterior aspect of the anastomosis, while it results in rapid and surpassingly excellent healing, is essentially impracticable because it does

not produce hemostasis and is difficult to place accurately, while practically equally good healing is obtained by the use of the ordinary continuous through-and-through circular suture (posterior method 5). The latter does not cause the undesirable complications here that occur when it is used on the anterior aspect of the anastomosis.

As far as remote results are concerned, in our specimens after ninety days of healing, we could see no distinctive difference in the healing

Fig. 10 (dog 70, anterior method 7, nine day healing period).—A section showing remarkable mucosal restitution at *a*. The small cystic areas opposite *S* indicate an area of gastric mucosa damaged probably from our catgut suture. This appearance is characteristic of trauma by suture (probably also of any other type of light mechanical trauma) to either gastric or intestinal mucosa. At *c* is a silk suture defect with a surrounding inflammatory reaction. This also involves *b* where the silk lies in a space lined by intestinal mucosa (suture inclusion) (fig. 11). *I* indicates intestine.

which followed the use of the lock-stitch suture and that which followed posterior methods 5 and 7 as the innermost posterior layers. It will be remembered that healing after the lock-stitch suture, as reported in

our previous study, was complicated by an appreciable loss of mucosa and considerable inflammatory reaction at and about the point of gastro-intestinal apposition during the early stages of healing. In all our specimens after ninety days of healing the muscularis mucosae remained separated by a definite zone of fibrous stroma. However, the other muscular layers in some specimens, particularly after posterior method 7, showed such little intervening fibrous stroma that it was difficult to see. In other specimens gastric and intestinal muscularis were separated by an easily distinguishable zone of connective tissue.

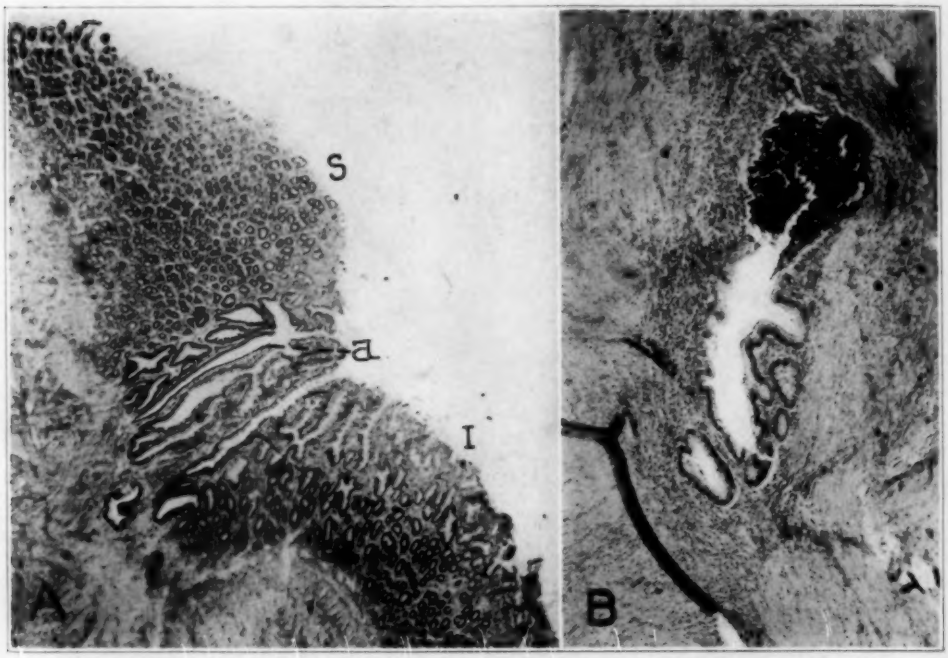

Fig. 11.—*A* is a higher magnification of the corresponding area in figure 10. The exact point where the gastric (*S*) and intestinal (*I*) mucosa meet is shown at *a*. *B* is higher magnification of the area *b* in figure 10.

THE FATE OF SILK SUTURES

This was considered in our former study and we shall consider here only the fate of silk sutures in the eight animals in which there was a healing period of ninety days. Histologic study of the material from the anterior aspect of the gastro-intestinal ostium showed silk suture material in six of the eight specimens. In one a mucosal inclusion was seen about the silk and in two others this was questionable. In five of the six specimens in which silk was observed there was a well defined active inflammatory reaction about the silk, and in three (nos. 57, 66

and 69) this was associated with chronic peritonitis. It could be definitely observed that silk was escaping into the gastro-intestinal lumen in two animals. In the others it was debatable in which direction the silk was moving; however, in view of the associated inflammation we suspected that the intestinal mucosa had been damaged and that the silk would ultimately find its way into the gastro-intestinal lumen.

A study of the posterior aspect of the gastro-intestinal ostium in seven specimens offered an interesting contrast. It will be remembered that posterior suturing was done by placing first a continuous circular serosubmucosal suture of 0 black silk with a curved intestinal needle on a needle holder. In other words, this silk suture was not placed by the most desirable technic. The second posterior suture was placed after the stomach and intestine were opened and in five animals consisted of a continuous lock-stitch suture of 00 plain catgut that traversed the entire thickness of the wall of the stomach and intestine, while in two animals this second row of catgut suture was merely a continuous circular suture that passed through the serosa and muscularis, possibly some submucosa, but avoided the mucosa.

Remains of silk sutures were seen in all seven specimens after posterior suture, and in none was an associated mucosal inclusion observed. In two specimens there was evidence of an active inflammatory process about the silk, in each of which it was suspected that the silk was migrating toward the intestinal lumen, and in one there was associated questionable chronic peritonitis. In the five remaining specimens the silk was obviously migrating toward the serosa, frequently being seen in the subserosa and unassociated with any evidence of active inflammatory reaction such as lymphocytes and polymorphonuclear leukocytes.

It therefore appears that 0 silk suture material may persist in a gastro-intestinal anastomosis for ninety days or more after operation and that the question of its being associated with an active inflammatory process depends probably on a complicating mucosal injury. In the latter event the suture probably eventually escapes into the gastro-intestinal lumen.

It may seem strange that the posterior silk sutures which were placed with a curved needle on a needle holder were associated with fewer complications (inflammation, mucosal inclusions, discharge into the gastro-intestinal lumen) than the anterior silk sutures which were threaded on straight milliner's needles and placed directly by hand without a needle holder, which is the more ideal method. Here again our explanation is that it is difficult to place a serosubmucosal suture accurately when suturing has to be done at right angles to a ridge, as occurs particularly when suture method 5 is used anteriorly. It is then difficult to place a second row of mattress sutures close to such a distor-

tion without piercing the intestinal mucosa. Burget and one of us (K. H. M.) [5] had a corroborative experience in an earlier study. The wall of the stomach, because of its greater thickness, does not offer the same technical hazard.

SUMMARY AND CONCLUSIONS

This study is based on experimental observations on twenty dogs. Anterior gastroduodenostomies and jejunostomies were performed by two suture methods while the suture material was uniform throughout. We were unable in this study as in our previous one to demonstrate the occurrence of serosal cysts between the two apposed serosal surfaces of a gastro-enterostomy.

Mucosal inclusions in the anterior line of gastro-intestinal apposition were frequent occurrences in this, as in our previous, study when suture methods were employed that evert the mucosa between the walls of the stomach and intestine. The only method employed for this purpose was a through-and-through continuous circular suture (method 5) recommended in numerous textbooks of surgery.

Inclusions so produced may persist for ninety days or longer and may or may not communicate with the gastro-intestinal lumen as demonstrated by serial sections. When such communication fails the mucosal inclusion becomes distended to form a cyst of appreciable size. Inflammatory phenomena may also accompany such appositional inclusions.

Suture methods that produce such inclusions, therefore, are faulty in that they produce anomalies and complications that can only be regarded as undesirable. In view of this experience we reiterate the conclusions expressed in our previous study that the recommendation of some authors to use suture methods that evert gastro-intestinal mucosa for purposes of hemostasis is dubious advice.

The use of a two layer serosubmucosal suture technic (method 7) as proposed by us is practical and largely eliminates the faults of the other multilayered suture methods commonly used on the anterior aspects of gastro-enterostomies. It also permits exceptionally rapid healing and confirms our earlier observation that separate suture of the mucosa (mucosa and submucosa) is wholly unnecessary for rapid healing since it actually retards rather than hastens mucosal restitution.

This study confirmed our previous observations on the use of silk suture material in gastro-enterostomy. When so placed that they do not penetrate the mucosa silk sutures are ideal, for they produce a minimal inflammatory reaction. However, when they penetrate the

5. Martzloff, K. H., and Burget, G. E.: The Closed Intestinal Loop: III. Aseptic End-to-End Intestinal Anastomosis and a Method for Making a Closed Intestinal Loop Suitable for Physiologic Studies, Arch. Surg. **23**:26 (July) 1931.

intestinal mucosa, as occasionally happens even in expert hands, they become complicated by infection and inflammation and often by mucosal inclusions (suture inclusions), all of which may persist for ninety days or longer. We therefore doubt the advisability of using silk suture material in gastro-intestinal anastomosis.

NOTE.—A recent experimental study by Nogara (Nogara, G.: Sulle modalità di cicatrizzazione delle ferite chirurgiche dello stomaco in rapporto alla technica di sutura impiegata, Arch. ital. di chir. **36**:111, 1934) reveals the use of a sero-submucosal suture (Donati) which, while slightly differently placed than our stitch, nevertheless, embodies the same principles. Nogara reported excellent healing of the wound with this extramucosal suture as compared with the results of other methods and confirmed our experience that separate suture of the mucosa is not a requisite for rapid uncomplicated healing.

EVENTRATION OF THE DIAPHRAGM

WITH A REPORT OF TWO CASES

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Eventration of the diaphragm is rare, and because of this fact we feel that every case is worthy of detailed study. It also seems desirable to review the literature.

The purpose of this paper is (1) to summarize the available knowledge of the disease with a discussion of the literature and (2) to present reports of 2 cases.

REVIEW OF THE LITERATURE

THE NAME

Eventration of the diaphragm clinically has come to mean a congenital or, occasionally, an acquired high or elevated position of one leaf of the diaphragm muscle, characterized pathologically by aplasia or atrophy of the muscle fibers of the affected side but with no break in the continuity of the muscle, which in the vast majority of cases produces symptoms suggesting a gastric, cardiac, pulmonary or pleuropulmonary origin.

The term eventration has been objected to by many on the grounds that the derivation of the word, namely, "e," meaning out, and "venter," meaning belly, in no sense gives an impression of the true pathologic process. The term apparently inappropriately describes the condition which exists. Königer [1] suggested the term idiopathic high-lying diaphragm. Other names suggested have been high diaphragm, relaxed diaphragm and insufficiency of the diaphragm, as listed by Reifenstein; [2] Lerche [3] preferred insufficiency; Hillejan [4] called the condition relaxation of the diaphragm and Bierman [5] described his case as one of "idiopathic eventration," presumably by inference suggesting another

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1. Königer: München. med. Wchnschr. **56**:282, 1909.
2. Reifenstein, E. C.: Am. J. M. Sc. **169**:668, 1925.
3. Lerche, W.: Surg., Gynec. & Obst. **34**:224, 1922.
4. Hillejan, A.: Zentralbl. f. Gynäk. **47**:1383 (Aug.) 1923.
5. Bierman, M. I.: Radiology **4**:122 (Feb.) 1925.

type having a known origin. Goriainova [6] did not suggest the use of any particular name but discussed at some length the question of a name, calling attention to the work of Wieting, who suggested the term relaxation, of Leichtenstein, who called the condition "a high level of the diaphragm," and of Morrison,[7] who felt that "Petit's disease" would pay full tribute to that eminent eighteenth century surgeon who is given credit for first describing the condition. In Lord's [8] article it was suggested that the condition be called elevation of the diaphragm, the derivation of the word again being cited.

It is well known that the term is incorrectly used and is a misnomer. If the original *eventratio diaphragmatica* were translated to be diaphragmatic eventration and interpreted to mean the belly (abdominal organs) moving out of its usual position and in a diaphragmatic direction there might be some justification for the term. We believe with others that it is to be regretted that the term eventration of the diaphragm has crept into the literature, but as the intended meaning is usually well understood it might be confusing to change; so usage condemns the term to remain.

HISTORY

The first authentic case was described by Petit [9] after a postmortem examination. The report of this case appeared in a posthumous edition of the author's work published in 1774 and edited by his pupil Lesne. Korns [10] called attention to the fact that Bowditch in 1853 mentioned Senac's case (1729) as being in all probability a genuine instance of eventration, but after reference to the original article Korns stated that such a conclusion was not justifiable in his opinion. In connection with the report of Petit's case it is of considerable interest to note the inaccuracies that are found in the literature and that are repeated even after a correction is made. For instance, many writers have credited Petit with reporting a case in the literature as well as with naming the condition. Beck [11] and others have stated that Petit reported his case in 1790. Jean Louis Petit was born on March 13, 1674, and died on April 20, 1750, nearly twenty-five years prior to the appearance of the report of the case in the literature. There were apparently four editions

6. Goriainova, R. J.: Vestnik roentgenol. i radiol. **6**:257, 1928.

7. Morrison, J. M. W.: Arch. Radiol. & Electroth. **27**:353 (May) 1922.

8. Lord, F. T.: Eventration of the Diaphragm, Arch. Surg. **14**:316 (Jan.) 1927.

9. Petit: Traité des maladies chirurgicales, Paris, T. F. Didotjeune, 1774, vol. 2, p. 266.

10. Korns, H. M.: Diagnosis of Eventration of the Diaphragm, Arch. Int. Med. **28**:192 (Aug.) 1921.

11. Beck, H. G.: Ann. Clin. Med. **1**:262 (May) 1923.

of his work. The first three were edited by Lesne and appeared in 1774, 1780 and 1790, respectively, while the fourth edition, edited by Sansom, was published in 1837.

The name eventration was given to the disease by Beclard, mentioned in the writings of Cruveilhier.[12] Wood and Wood[13] mentioned that Petit gave the name eventration to the condition, but this is apparently erroneous, as Petit made no reference to the term in his published writings. Korns substantiated the latter view, and one is inclined to agree with him, as his critical review is a splendid piece of material.

Marsh[14] in 1867 reported the first instance of a clinical examination and a correlation of clinical signs and autopsy observations. Reports of roentgen studies in cases of eventration began to appear about 1901. Widenmann[15] has been credited by some[13] with being the first to use roentgen rays in diagnosing the disease, while others have mentioned Struppler[16] as the first to rely on roentgen study. This confusion is undoubtedly due to a difference in the date of their publications, as Widenmann reported his studies in March 1901 and Struppler published his report in May of the same year.

Historically, the celebrated case of Freidrich Schneider is of much interest. This case was first mentioned in 1890 by Stinzing, according to Neumann.[17] From this time until 1912 the patient Schneider presented his diagnostic problem at many clinics. Hirsch[18] in 1900 examined him and from roentgen studies made a diagnosis of hernia of the diaphragm. Volkmann and Becker saw the patient and made a diagnosis of dextrocardia, according to Glässner.[19] In 1905 Hildebrand and Hess[20] first established a diagnosis, depending on Schlippe's procedure of measuring respiratory variations with intragastric pressure. Lotze[21] in 1906 confirmed Hirsch's diagnosis of hernia. In 1912 von Eggling[22] made a report of the necropsy observations which supported the diagnosis of Hildebrand and Hess of eventration.

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12. Cruveilhier: Anatomie pathologique du corps humain, Paris, J. B. Baillière, 1829, vol. 1, book 17; Traité d'anatomie pathologique générale, Paris, J. B. Baillière & fils, 1849, vol. 1, p. 614.

13. Wood, W. B., and Wood, F. G.: Lancet **2**:392, 1931.

14. Marsh: Lancet **1**:298, 1867.

15. Widenmann: Berl. klin. Wchnschr. **38**:279, 1901.

16. Struppler: Deutsches Arch. f. klin. Med. **70**:1, 1901.

17. Neumann: Deutsche med. Wchnschr. **45**:905 and 937, 1919; München. med. Wchnschr. **64**:719, 1917.

18. Hirsch: München. med. Wchnschr. **47**:996, 1900.

19. Glässner: Fortschr. r. d. Geb. d. Röntgenstrahlen **24**:208, 1916; München. med. Wchnschr. **63**:19, 1916.

20. Hildebrand and Hess: München. med. Wchnschr. **52**:745, 1905.

21. Lotze: Deutsche med. Wchnschr. **32**:1662, 1906.

22. von Eggeling: München. med. Wchnschr. **59**:2284, 1912.

A case of eventration on the right side was first reported by Wieting [23] in 1906, in which there was associated hernia of the left leaf of the diaphragm. This, to the best of our knowledge, is the only case of its kind reported. Eppinger [24] in 1911 described the second case of eventration on the right side; Glässner in 1916, the third, and Bayne-Jones [25] in 1916, the fourth. The last-mentioned was the first case of eventration on the right side to be reported in the American literature and the second on either side, Sailer and Rhein [26] reporting the first in 1905.

The searching critical review by Korns [10] contained several points of interest: First, it was a résumé of all the literature on the subject up to the time of writing, analytically studied and severely criticized for errors, with corrections of the same errors. Second, special attention was given to the diagnosis of the condition. Third, interest was aroused in the condition from a physiologic standpoint when the author described a diagnostic sign based on the function of respiration and the anatomic structures involved therein. Fourth, the first case of definite associated aplasia of the lung on the involved side was presented. Much credit is due Korns for this article.

ETIOLOGY

There is no specific cause demonstrable for eventration of the diaphragm. It is apparently congenital, although many instances have been cited of cases of an acquired condition and of a condition associated with other pathologic conditions if not actually produced by them. The early literature on the etiology pointed more to its congenital nature, while reports of the past ten years seem to substantiate the theory of the acquired nature of the disease. Reich, quoted by Goriainova,[6] stated that eventration must be definitely and clearly distinguished from the high diaphragm produced by paralysis of the phrenic nerve, that by the term eventration of the diaphragm should be understood a high level of the diaphragm resulting from atrophy and degeneration of the musculature and that all cases in which there is injury of the phrenic nerve, due to trauma, pathologic changes in the lung and infectious processes, must be excluded. Some confusion seems to exist relative to the etiology, but we are of the opinion after a critical search of reported cases that we must accept the etiologic grouping of both congenital and acquired types.

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23. Wieting: Deutsche Ztschr. f. Chir. **82**:315, 1906.

24. Eppinger: Allgemeine und spezielle Pathologie des Zwerchfells, in Nothnagel, C. W. H.: Spezielle Pathologie und Therapie (supp.), Vienna, A. Hölder, 1911.

25. Bayne-Jones, S.: Eventration of the Diaphragm, Arch. Int. Med. **17**:221 (Feb.) 1916.

26. Sailer, J., and Rhein, R. D.: Am. J. M. Sc. **129**:668. 1905.

Theory of Congenital Origin.—The supporters of the theory of the congenital origin of eventration advance the following to substantiate their belief: first, the relative frequency of occurrence on the left side; second, the frequency of occurrence in the fetus and in new-born and young children; third, associated congenital anomalies, and, fourth, the absence of symptoms for a long time.

Of a total of 183 cases reviewed (65 reported by Korns and 118 reviewed from original sources by us) the left leaf of the diaphragm was affected in 165 and the right leaf in 18. Reifenstein and others suggested the protection of the liver as a possible reason for the preponderance of the condition on the left side and further advanced the suggestion that the left leaf is the last to close. Embryologically one may look to the blood supply of the developing organs. Cutler and Cooper,[27] in discussing this aspect of such deficiencies, called attention to the fact that the rôle of the liver as a protecting organ to the right side is an inadequate reason as the liver is formed under the septum transversum and during a large part of embryonic life protects the left side as much as the right. Also, they expressed the belief that the explanation of the preponderance of diaphragmatic lesions on the left side lies in the distribution of the vascular elements which play such an important rôle in the early formation of the embryo. Supporting this contention they advanced the following embryologic facts: First, the position of the pulmonary ridge of Moll and the pleuroperitoneal membrane is determined by the common cardinal veins. In the human embryo measuring 20 mm., the common cardinal vein on the right grows and forms the superior vena cava, while that on the left atrophies and disappears. It seems that this would cause a tendency to weakness of the left pleuroperitoneal membrane. Second, in the embryo measuring 2.5 mm. the liver becomes adherent to the wall of the dorsal body on the right to allow for the formation of the vein of the placa vena cava, which becomes the inferior vena cava. Third, in the embryo measuring 3.5 mm. the tubal heart loops over to the right preparatory to the formation of the atria and ventricles. Fourth, in the embryo measuring 4.5 mm. the right half of the sinus venosus is observed to be growing much faster than the left. It seems possible that the vascular concentration in the region of the right side of the diaphragm would contribute to the strengthening and blocking of the pleuroperitoneal canal, while the atrophy of the common cardinal vein on the left would contribute to the weakening of the left half of the diaphragm.

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27. Cutler, E. C., and Cooper, H. S. F.: Congenital Deficiency of the Diaphragm, Arch. Surg. **8**:506 (March) 1924.

In one group of 83 cases reported since 1921 were 30 cases of patients under 25 years of age, distributed according to age groups as follows:

Age	No. of Cases	Age	No. of Cases
New-born	5	10 years	3
1 year	2	11 years	2
2 years	1	12 years	2
3 years	1	14 years	2
5 years	1	16 years	2
6 years	1	21 years	2
8 years	2	22 years	1
9 years	1	23 years	1

This frequency of occurrence in the new-born and in young children seems to support the theory of a congenital origin.

The association of other congenital conditions increases the value of this theory. The presence of such conditions has been reported by many authors. Transposition of one or more of intra-abdominal organs was reported by Morris,[28] Lord [8] and others. Megacolon was present in the cases of eventration reported by Aronson and Quénu and Fatou.[29] Other abnormalities reported were aplasia of the lung,[30] hypospadias, undescended testis,[31] abnormally lobulated lungs,[25] rotation of the esophagus,[21] aortic hypoplasia and pseudolobulation of the upper lobe of the lung,[32] reduction in the size of the phrenic nerve and esophageal diverticula [33] and nonrotation of the stomach.[34] Uniform absence of evidence of compression of the contiguous lung has been emphasized as one of the strongest arguments in favor of congenital etiology of eventration of the diaphragm. Byloff, cited by Bayne-Jones,[25] spoke of eventration as a stigma of degeneration.

The absence of symptoms for a long time with the finding of such a marked chronic pathologic process has been offered by some as evidence of a congenital lesion. It is inferred that if this were an acquired disease symptoms should begin at the time of onset in all cases. In Whittington's [35] patient, aged 64, the symptoms began rather suddenly and the previous history was irrelevant in every respect, while in Thomp-

28. Morris: Brit. J. Radiol. **2**:85, 1929.

29. Quénu, J., and Fatou, E.: J. de chir. **24**:1 (July) 1924.

30. Caussade and Fatou: Bull. et mém. Soc. méd. d. hôp. de Paris **52**:246, 1928. Korns.[10]

31. Hess, J. H.: M. Clin. North America **8**:567 (Sept.) 1924.

32. Vigetti: Rev. méd. del Rosario **18**:502 (Dec.) 1928.

33. Marchal, Fatou and Heim de Balzac: Bull. et mém. Soc. méd. d. hôp. de Paris **48**:795, 1932.

34. Harris, L. I., and Stivelman, B. P.: Nonrotation of Stomach Simulating Spontaneous Hydropneumothorax, J. A. M. A. **89**:1836 (Nov. 26) 1927.

35. Whittington: Boston M. & S. J. **190**:244, 1924.

son's [36] patient, aged 54, the sudden onset of symptoms suggested cardiac failure. In Madinaveitra's [37] case the patient, aged 63, complained of mild indigestion for twelve years with an acute increase in the gastric symptoms of only six months' duration. Fatou and Heim de Balzac [38] reported the case of a patient, aged 59, whose symptoms began with an acute pain which simulated that of angina. Such examples illustrate the delayed onset of symptoms in cases of eventration proved to be congenital by pathologic study.

Theory of Acquired Origin.—Trauma, toxic origin from acute infectious diseases, pulmonary tuberculosis, subphrenic abscess, tumor of the mediastinum, chronic gastric disturbance, lesions of the phrenic nerve other than traumatic, pregnancy, thoracic growth, aneurysm of the aorta and subdiaphragmatic hydatid cyst have been reported in the literature as being either causative or associated factors. Reported cases illustrate these contentions. Lerche, although not reporting specific cases, mentioned typhoid, diphtheria, septicemia, nephritic erysipelas, pericarditis, endocarditis, rheumatic fever, Huntington's chorea, alcoholic neuritis, fracture or luxation of the spinal column, spondylitis, pachymeningitis, spinal hemorrhage and tumor of the spinal canal as etiologic background for eventration.

Cruveilhier first mentioned trauma as the cause of eventration. Neumann in 1919 suggested injury of the phrenic nerve. Allan [39] in giving the history of his patient mentioned that pain came on suddenly after the cranking of an automobile and that the patient had "ruptured both sides." Wheatley's [40] patient was in an automobile accident which suggested traumatic origin, but the author did not conclude that it was the causative factor. Bamber,[41] Bulmer [42] and Vigetti mentioned lifting of heavy objects in the history of their patients. In the case reported by Bulmer there was an associated gastric ulcer, while in Vigetti's case there were pulmonary tuberculosis and hypoplasia of the aorta. Fatou and his associates [43] stated that the patient whose case they reported had a history of thoracic contusion on the right side with symptoms dating from the time of the accident, but the left leaf of the diaphragm was elevated. D'Pierron's [44] patient was a man, aged 34, who had been

36. Thompson, A. P.: Birmingham M. Rev. **5**:44 (Feb.) 1930.

37. Madinaveitra: Progresos de la clín. **35**:243 (April) 1927.

38. Fatou and Heim de Balzac: J. de radiol. et d'électrol. **16**:491 (Oct.) 1932.

39. Allan, W.: Virginia M. Monthly **47**:305 (Oct.) 1920.

40. Wheatley, F. E.: Boston M. & S. J. **197**:87 (July 21) 1927.

41. Bamber, J. M.: M. Clin. North America **2**:771 (Nov.) 1927.

42. Bulmer: Birmingham M. Rev. **5**:48 (Feb.) 1930.

43. Fatou; Prévost, L., and Prévost, F.: Bull. et mém. Soc. méd. d. hôp. de Paris **52**:259, 1928.

44. d'Pierron: Arch. d'électric. méd. **39**:322 (Aug.) 1929.

well until a fall six months previously, after which there was extreme dyspnea with suffocation, which continued. During the fall there was severe compression of the stomach, and the author believed that this was the etiologic factor. Wood and Wood mentioned trauma and cited a case but said there was only a temporary elevation. Kromeke, cited by Goriainova, explained the more frequent involvement of the left cupola by the peculiarity of the course of the left phrenic nerve, which runs definitely more anterolaterally than the right one for one seventh of its course and unwinds not only on the superior surface of the left leaf but also on the under-surface and therefore is more prone to trauma than the nerve on the right side.

Toxic origin from acute infectious diseases is a relatively rare occurrence. Fischer [45] mentioned a case in which eventration developed during convalescence from double pneumonia and typhoid, but no other cases have been found on careful search of the literature with the exception of a case reported by Goriainova in which symptoms appeared after an attack of measles.

Pulmonary tuberculosis has been noted in a number of cases of eventration. The exact relationship has not been definitely established. Morrison [46] in reporting 9 cases of paralysis of the phrenic nerve stated that the elevation of the diaphragm was due to a pathologic lesion involving this nerve and producing roentgenographically a picture synonymous with that of Petit's eventration. The first case he mentioned was that of a man 58 years old who had bronchitis and pulmonary tuberculosis; on postmortem examination the phrenic nerve was found to be involved in a mass of fibrous tissue. In the ninth case there was extensive tuberculosis of the left lung and to a lesser extent of the right lung with the left side of the diaphragm elevated and partially fixed. Caussade and Fatou performed an autopsy in a case in which they had diagnosed the condition three months previously as eventration and bilateral tuberculosis and confirmed their clinical impressions; they likewise found a congenitally dwarfed left lung. They concluded that eventration is not infrequent in tuberculous persons. In a second case reported by the same authors [47] the condition was clinically diagnosed as eventration and tuberculosis, although the report was admittedly incomplete. Goriainova's patient, in whom symptoms appeared following an attack of measles, had tuberculous broncho-adenitis. De Lacerda's [48] first patient had been perfectly well up to five months prior to consultation and then began to have hemoptysis followed in a few days by cough, which caused acute sharp pains at the base of the left lung.

45. Fischer, H.: M. Rec. **86**:653, 1914.
46. Morrison: Arch. Radiol. & Electroth. **28**:72 (Aug.) 1923.
47. Caussade and Fatou: Bull. et mém. Soc. méd. d. hôp. de Paris **52**:254, 1928.
48. de Lacerda: Lisboa méd. **5**: 213 (April) 1928.

The sputum gave a positive reaction to Koch's organism, and the diaphragm was elevated on the left. The second case reported by the same author was that of an army officer, aged 36, who for ten months had a clinical history of tuberculosis and an intense pain in the epigastrium and at the base of the thorax on the left side which seemed to be related to the ingestion of food. There was a previous history of syphilis. A diagnosis was made of eventration and pulmonary tuberculosis with a positive reaction of the sputum. Labbé and his co-workers [49] reported a case of eventration, pulmonary tuberculosis and partial pneumothorax in the same patient. In an autopsy report [50] made about a year later they confirmed the clinical observations and concluded that the eventration was probably not congenital but secondary to the pulmonary infection. It is rather interesting that Labbé [51] reported the same case again, thereby giving rise to some confusion until careful investigation revealed it to be the same. Vigetti's case, which has been noted previously, was terminated by a "galloping type of consumption," but the author concluded because of the congenital abnormalities found at autopsy that the tuberculosis was secondary and terminal. Allan's patient, mentioned earlier, was found on roentgenologic study to have a tuberculous focus in the apex of the right lung, and he died one year later of pulmonary tuberculosis.

Chronic gastric disturbance was noted in a number of cases of eventration. The associated lesions mentioned most often were peptic ulcer and gastric carcinoma. Quénu and Fatou [20] were emphatic in their statement that gastric lesions do not cause eventration but that, on the contrary, eventration predisposes one to organic lesions of the stomach. Their contention was not substantiated further than by the citation of the occurrence of cancer or ulcer in 11 of 18 cases in which there was surgical intervention. Buono [52] felt, however, that ulcerative and neoplastic diseases of the stomach cause superelevation of the diaphragm. Golob's [53] patient, who was operated on by Lilienthal, had a carcinoma at the cardiac end of the stomach with eventration on the right side. The patient in the seventh case of Morrison's first series [46] had a cancer of the stomach, but the diaphragm was only slightly elevated, and one would doubt from the description that this was a true case of eventration. Verbrycke [54] reported the case of a patient with perforated ulcer high on the lesser curvature of the stomach and

49. Labbé, M.; Boulin, R.; Azérad, E., and Soulié, P.: Bull. et mém. Soc. méd. d. hôp. de Paris **54**:830, 1930.

50. Labbé: Bull. et mém. Soc. méd. d. hôp. de Paris **47**:468, 1931.

51. Labbé: Arch. de mal. de l'app. digestif **23**:241 (March) 1933.

52. Buono: Riv. di radiol. e fis. med. **2**:118 (March) 1930.

53. Golob, M.: M. J. & Rec. **124**:473 (Oct. 20) 1926.

54. Verbrycke, J. R., Jr.: Surg., Gynec. & Obst. **40**:415 (March) 1925.

a high diaphragm or, more accurately from the description given, a localized eventration. However, the subsequent history and the roentgenograms submitted cast some doubt on the authenticity of the case as one of true eventration.

Causation by or association with other conditions is less rare. Goriainova mentioned injury to the sympathetic nerve endings as a possible cause. He cited Hoffman and several other authors as believing aerophagia to be an etiologic factor. Jawara and Dumitresco-Mante [55] noted a case of considerable interest in which a hydatid cyst was found under the diaphragm on the right side at operation and was drained and sutured. About two weeks later roentgen study demonstrated an elevation of the diaphragm on the right side with apparent fluid in a new cyst, which was aspirated. Two years later the authors reported the patient cured, but stated that the movement of the diaphragm was reduced; they concluded with a question as to whether this was a case of true eventration or only of distention.

After a study of cases reported in the literature we feel that the weight of evidence seems to be undoubtedly in favor of a theory of congenital origin, but some few cases presented in favor of an acquired nature bear evidence of careful consideration and cannot be overlooked.

Embryologic developmental defects are always rare, and eventration of the diaphragm is a relatively rare condition. The last critical review of the literature, made by Korns in 1921, included 65 cases. Since that time we have been able to find 118 cases reported in the literature, bringing the total to 183, including our own cases reported in this communication. Korns divided his cases into two groups: (1) those in which the diagnosis was regarded as proved, and (2) those in which the diagnosis was not proved but was regarded as reasonably certain. His standard of measurement was strict. The cases in the first group included those in which the diagnosis was substantiated by necropsy, operation or the physiologic study of the muscles of respiration, while those in the latter group were apparently all the others. Following Korns' plan we have tabulated the cases as follows:

	Incidence	
	Left Side	Right Side
Korns' collection		
Group 1	18	4
Group 2	41	2
Subsequent cases		
Group 1	23	2
Group 2	83	10
Total	165	18

55. Jawara and Dumitresco-Mante: Rev. méd.-chir. d. mal. du foie **7**:105 (March-April) 1932.

In this grouping we have considered 3 of Lord's cases as belonging to group 1 and all of Uspensky's, as they demonstrated the presence of Hoover's or Korns' sign. One of our cases is in group 1, for the diagnosis was verified at operation, while our other case is in group 2. We have included in group 2, 22 of the 41 cases reported by Dillon and 8 of those in Morrison's series of cases associated with injury to the phrenic nerve, 1 falling into group 1 because the diagnosis was proved at autopsy. The condition in Dillon's cases and in some of Morrison's might be questioned as not being true eventration but rather rudimentary elevation. We have felt that with this explanation we could include them in this study as cases of eventration.

Occurrence.—Lord mentioned finding only 4 instances in the course of 16,504 roentgen examinations at the Massachusetts General Hospital. It is believed, however, that eventration is not as rare as this report would indicate for there are cases which have never been recorded in the literature.

Eventration seems to occur more frequently in males than in females. Walton [56] said that it occurs four times more frequently in the former than in the latter. It is not known on what basis these data were presented; we have not been able to confirm such a preponderance. In the group of cases we have reviewed the ratio was approximately 4:3 in the cases in which the sex was given. In a number of cases of eventration occurring in the new-born the various authors did not mention the sex. Whittington mentioned the fact that roentgenologists believe it to be more common than the literature suggests.

PATHOLOGY

The pathologic observations in this disease might be placed in two groups: the changes in the diaphragm and the associated or accompanying pathologic process.

The diaphragm has been variously described, but there is no adequate and detailed picture in any of the reports, and microscopic study of sections is totally lacking. In all cases the diaphragm was found definitely and markedly elevated. In a few reports a rudimentary eventration was mentioned, meaning apparently a moderate elevation, but these few cases are not considered by us as true examples of the condition and therefore have been dropped from the group. Bayne-Jones' discussion of the pathology is quite complete. His report was based on a study of 22 cases which came to autopsy or operation and therefore should be considered as fairly reliable examples. He stated that in all cases there was a thin translucent membranous diaphragm. It was usually a layer of fibrous tissue containing some muscle fibers,

56. Walton, H. J.: Am. J. Roentgenol. **11**:420 (May) 1924.

but in a few there was only a thin aponeurotic sheet. The diaphragm was opaque and whitish as distinguished from the red of normal muscle tissue. Sailer and Rhein mentioned the microscopic observation of numerous muscle fibers, although on gross examination their absence was noted, while Wieting spoke of the diaphragm as a fascia-like structure without muscle fibers. Benda mentioned lipomatous pseudohypertrophy of the diaphragm. Motzfeldt [57] said that the diaphragm showed atrophy and fatty changes. Verbrycke in his cases found a bluish-gray, very thin diaphragm which apparently lacked tone, while in 1 of Morrison's cases that came to operation there was a thinned out diaphragm of dense fibrous tissue. In our own case, as will be seen in the surgical report, there was a much thinned out diaphragm which was tense at all times. Eggers [58] demonstrated in his case localized eventration at the central tendon without, of course, a rent in the diaphragm. This last case is the only one of its kind reported in the literature.

Pathologic change in the phrenic nerve on the side affected has been noted. Bayne-Jones stated that the phrenic nerve may be reduced in size, but that it contains normal fibers with no evidence of degeneration in the nerve trunk or its nuclei. Marchal and his associates mentioned the reduction in the size of the phrenic nerve, but this was a quotation and not an observation on any of his presented cases. Morrison reported 9 cases of paralysis of the phrenic nerve in which the nerve was involved in a mass of fibrous tissue, while in another case the nerve was involved in a nodule of carcinoma; full descriptive postmortem studies were conspicuously absent. Hess spoke of injured phrenic nerves and anomalies, but we are unable to find any such pathologic process described in reported cases aside from the aforementioned suggestion.

The lungs show no evidence of compression. Abnormally lobulated lungs have been reported. Korns reported that his case was "the first in which aplasia of the lung has been shown to accompany the condition of eventration of the diaphragm." Vigetti, in a splendid necropsy report, found the lung on the affected side "reduced in size with a pseudolobulation of the upper lobe." Pulmonary tuberculosis is frequently associated with the condition, and in a case of Labbé's pneumothorax was present.

The heart and mediastinum in eventration on the left side are displaced from the usual position to the right side; no mention has been made in the reported cases of the position of these structures in eventration on the right side. A number of writers have persisted in calling this dextrocardia, but most recent authors have confirmed the impression

57. Motzfeldt: Deutsche med. Wchnschr. **57**:1006, 1910.

58. Eggers, C.: J. Thoracic Surg. **1**:41 (Oct.) 1931.

that there is rotation of the heart rather than true transposition of that organ.

Other pathologic changes and associated diseases noted are: Hirschsprung's disease, dilatation and malformation of the mesentery, transposition of the stomach and colon, familial hernia, intestinal obstruction, emphysema, atelectasis, bronchitis, asthma, ascites, malnutrition, ectopic testis, gastric volvulus, esophagotracheal fistula, aneurysm of the aorta, hypoplasia of the aorta, carcinoma of the mediastinal glands, neoplasm of the lungs, ulcerative colitis, esophageal diverticulum, subdiaphragmatic hydropneumocyst, hypospadias, diphtheria, poliomyelitis, progressive spinal muscular atrophy, influenza, nephritis and other infectious diseases.

SYMPTOMATOLOGY

Usually the symptoms appear insidiously and are of varying duration, but occasionally the onset is sudden.[34] The duration of the symptoms according to a study of cases abstracted from the literature is from two weeks to twenty years from the time of onset.

Symptoms vary tremendously and are not characteristic, but they are suggestive of the location of the lesion. There may be no definite symptoms.[58a] Symptoms may be divided into four groups: (1) respiratory, (2) gastro-intestinal, (3) circulatory and (4) general. This grouping is submitted after a careful study of the records of 118 cases reported since 1921. The gastro-intestinal and respiratory symptoms seemed to dominate the picture in a majority of cases.

Gastro-intestinal symptoms in the order of frequency were: pain in the abdomen, vomiting, pressure or weight in the stomach, gas, constipation, nausea, belching, loss of appetite, diarrhea, pain on swallowing, cramps and heart burn.

Respiratory symptoms in the order of their frequency of occurrence were as follows: dyspnea, pain in the chest, cough and wheezing.

Cardiac symptoms were: palpitation, cyanosis and tachycardia.

General symptoms were: loss of weight, fatigue or weakness, dizziness, sinking or fainting spells, pain down the arm on the affected side, malnutrition, edema of the lower extremities, insomnia, exhaustion, restlessness and numbness of the extremities.

It is undoubtedly true that the thoracic and abdominal symptoms were predominant in the majority of cases, although occasionally one sees a bizarre presentation of symptoms definitely suggesting other

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58a. Owen, C. C.: Radiology **18**:361 (Feb.) 1932. Uspensky: Brit. J. Radiol. **1**:197 (June) 1928. Blackford, L. M., and Booth, W. T.: Dextrocardia Secondary to Eventration of Diaphragm: Report of Asymptomatic Case, J. A. M. A. **98**: 883 (March 12) 1932. Foster, P. S.: Australian & New Zealand J. Surg. **2**:200 (Oct.) 1932. Morris.[28] Lord.[8]

diseases. Sometimes when other diseases are present the symptomatology of the latter is the main picture. It has been noted that displacement of the diaphragm leads to a displacement, and at times to a deformity, of all the organs in contact with the diaphragm, and therefore the symptomatology varies and depends on the organs plus the rapidity and extent of displacement. One author [59] grouped symptoms into those of dislocation, that is, symptoms arising from the dislocated organs, and those of dysfunction due to the improper function or the failure to function of the organs involved. In the order of frequency of occurrence by groups it was found in the cases reported and reviewed by one of us that the gastro-intestinal symptoms predominated, with the respiratory symptoms next and the cardiac symptoms last. A number of writers have placed various symptoms under different headings, which gives rise to some confusion in analyzing the cases for statistical comparison. For example, we placed dyspnea in the respiratory group as we felt that it is a pulmonary symptom due to pressure rather than one arising from cardiac pathologic change or dysfunction, although it is correctly pointed out by some authors that the heart is considerably more sensitive to any mechanical influence than are the lungs.

There are no unusual features of the gastro-intestinal symptom. They are the symptoms one would expect from displacement and dysfunction of the organs involved.

The symptom of pain in the chest, mentioned under the respiratory group, together with pain down the arm of the affected side, mentioned under the group of general symptoms, may lead one to suspect an anginal condition involving the coronary arteries. No such condition was reported in any of the autopsy observations in the literature.

PHYSICAL CHANGES

A summary of the typical but not pathognomonic observations elicited on physical examination may be given briefly: On general examination labored breathing, mild or severe, with some evidence of cyanosis suggests the possible thoracic location of the disease. The main physical signs are limited to the affected side of the thorax and the adjacent abdominal area. Inspection discloses diminished movement of the affected side, Litten's sign is absent, and Korns' or Hoover's sign is present. Palpation confirms the impression of diminished movement and the presence of Korns' or Hoover's sign and reveals diminished tactile fremitus at the base of the lung posteriorly on the involved side. The apex beat of the heart is difficult of palpation and when present is abnormally close to the left sternal border. The normal resonant percussion note over the lower third to the lower half of

59. Dillon: Ergebn. d. med. Strahlenforsch. **3**:289, 1928.

the lung on the side affected is absent. It is replaced posteriorly by a dull note and anteriorly by either a dull note or a definite tympanitic note, depending on the amount of fluid contained in the stomach at the time of the examination. A tympanitic note elicited anteriorly as high as from the fourth to the second left rib is quite suggestive of eventration on the left side. The percussion of the cardiac area of dulness in eventration on the left side demonstrates clearly that the right border of the heart is well beyond the right margin of the sternum while the left border is within the midclavicular or nipple line and may even be lost under the sternum. On auscultation the breath sounds and vocal resonance are usually diminished or absent over an area approximately corresponding to the height of the affected lesion of the diaphragm. Auscultation of the heart usually gives negative results, although there are reports of distant heart sounds, tachycardia, extrasystole and even auricular fibrillation, as shown in 1 of our cases. A succussion splash is usually evident and likewise a metallic tinkle or peristaltic gurgle over the lower anterior portion of the thorax on the side involved.

Scattered throughout the literature are numerous records showing departures from the usual physical changes just noted. In Bayne-Jones' case there was no displacement or evidence of enlargement of the cardiac area of dulness with eventration on the right side. Clopton [60] recorded normal physical changes except that the cardiac area of dulness was more to the right than in his first case. No physical changes in a case of eventration on the left side were reported by Morrison and Fatou and Heim de Balzac. Greenwald and Kaufman [61] reported no physical changes in a case on the right side. Caussade and Fatou reported the physical signs of pulmonary tuberculosis overshadowing all others or replacing the usual signs. Eggers stated that on inspection of the chest there was complete absence of expiratory excursion on the left side in a case of eventration of the left side of the diaphragm. Vigetti reported tachycardia in a case of eventration associated with tuberculosis. In a case of eventration on the right side Levick [62] noted a uniform enlargement of the left side of the chest anteriorly. Blackford and Booth frankly reported finding tympany over the affected portion of the chest anteriorly only on reexamination following roentgenologic study. Jewett [63] mentioned finding congestion of the superficial veins over the upper anterior surface of the wall of the chest. Harris and Stivelmann noted a lagging of the thorax on the right side with the

60. Clopton, M. B.: Ann. Surg. **78**:154 (Aug.) 1923.

61. Greenwald, H. M., and Kaufman, J.: Congenital Nonrotation of the Stomach with Eventration, Am. J. Dis. Child. **35**:641 (April) 1928.

62. Levick, G. M.: Proc. Roy. Soc. Med. **20**:1318 (July) 1923.

63. Jewett, C. H.: Clifton M. Bull. **8**:30 (Oct.) 1922.

lower interspaces on the same side, and the basal aspect of this side of the chest was more prominent in a case of eventration of the right side, while Allan reported that the left side seemed swollen and lagged on respiratory motion in a case of eventration on the left side. Prieto [64] noted the following changes in his case: The thorax in front showed marked deformity, the sternum deviating to the left; the thorax on the right appeared more ample, the intercostal spaces showed no modification and auscultation revealed distant heart sounds. The physical signs of pleurisy have been noted by many [65] and have been a source of error in diagnosis and medical management.

ROENTGENOLOGIC OBSERVATIONS

It is interesting to note that the roentgen ray has brought to light many cases of eventration but from the standpoint of diagnosis has added confusion and has given rise to numerous contradictory statements in the literature. After careful study we have reached the following conclusions regarding the roentgenologic observations: First, there are no pathognomonic roentgen signs, by which we mean there are no observations on which one can base a positive diagnosis; second, there are a number of signs which may make one strongly suspect eventration and on which one may even make a tentative diagnosis; third, many signs stated to be evidence of eventration undoubtedly occur both in eventration and in hernia, and fourth, there are a number of signs reported by various authors which apparently occur as coincidental findings.

Those signs which lend strong presumptive evidence to a diagnosis of eventration are: an unbroken curved convex line from the lateral wall of the chest to the mediastinum; the so-called "cup and spill," "cascade type" or bilocular stomach, with the level of fluid in the stomach after the ingestion of barium sulphate always coinciding with the esophageal opening when the patient is in the erect position; and the presence of a line above, the gastric bubble being to the medial side and the colonic bubble to the lateral side, which can be seen passing from one organ to the other forming a triangle below and between these two hollow organs.

The unbroken convex line so frequently mentioned is supposedly the intact smooth arch of the diaphragm. Dioclès and Orléan [66] in discussing this arched line stated that it may be the omentum or the walls

64. Prieto: Progresos de la clín. **41**:95 (Feb.) 1933.

65. Levine, S.: Ann. Int. Med. **5**:1000 (Feb.) 1932. Vigetti.[32] Thompson.[36] Allan.[39] Bamber.[41] Greenwald and Kaufman.[61]

66. Dioclès, L., and Orléan, E.: Bull. et mém. Soc. de radiol. méd. de France **19**:278, 1931.

of a hernial sac, as in Schoenfeld's case, or the wall of the stomach, and therefore is not to be relied on. Eggers, on the other hand, made a diagnosis by roentgenogram in his case of eventration based solely on this observation. Lord, in discussing this sign, cited the experience of Lotze, who made a diagnosis of eventration based on the unbroken line but at autopsy found diaphragmatic hernia. Reifenstein mentioned this sign as being fairly reliable, and Morrison rather emphatically called it one of the cardinal roentgenographic signs of eventration, yet one cannot well accept this as being authentic when he made a gross error in saying that until the time of writing eventration had occurred on the left side in all cases except that of Eppinger. Morrison must not have exhaustively reviewed the literature before publishing his résumé of the subject. Dillon mentioned the high unbroken arch as a characteristic sign and said that at times only a glance under the fluoroscope was sufficient to make the proper diagnosis; however, it is evident that in certain cases the diagnosis was associated with more difficulties. Lightwood [67] spoke of a "double convex parallel line" above the stomach as having considerable diagnostic value if present on repeated examination.

The so-called "cup and spill" type of stomach is caused by rotation on a fixed pivot which draws the greater curvature up under the diaphragm. The level of the fluid when barium is given always coincides with the esophageal aperture in eventration, whereas in hernia it is likely to be on a plane above this opening. Moore and Kirklin [68] corroborated this with the statement that it is a practical point in differentiation. Labbé mentioned this type of stomach as an inverted U stomach, while Jaubert de Beaujeu [69] spoke of it as a bilocular wallet stomach.

The convex line of the diaphragm stretching across from the air-filled colon to the stomach, forming a triangle below and between these organs, would, if constant, be a splendid presumptive finding in favor of a diagnosis of eventration.

There is much discussion in the literature regarding the movement of the diaphragm on the affected side. We feel that the movement may be normal, diminished, absent or reversed in either eventration or hernia. Reifenstein, Morrison and others have expressed the belief that paradoxical movement strongly suggests eventration, and Morrison went so far as to call it a cardinal sign of eventration. Reversed or paradoxical movement of the diaphragm is sometimes spoken of as Kienböck's phenomenon. Lord reported reversed movement on forced

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67. Lightwood, R.: Proc. Roy. Soc. Med. **26**:133 (Dec.) 1932.

68. Moore, A. B., and Kirklin, B. R.: Progressive Roentgenologic Diagnosis of Diaphragmatic Hernia, J. A. M. A. **95**:1966 (Dec. 27) 1930.

69. Jaubert de Beaujeu: J. de radiol. et d'électrol. **13**:508 (Sept.) 1929.

inspiration in his first case and limited but normal movement in his second and third cases, while Morrison found reversed movement in all of his cases. Bierman likewise reported limited but normal excursion and added that the leaf of the diaphragm on the unaffected side seemed to compensate for the affected leaf. Walton found normal diaphragmatic excursion in his case but stated that paradoxical movement was present in both hernia and eventration. Ottosen [70] examined his patient three years after his first observation and recorded accurate measurements of the movements of both leaflets of the diaphragm. He found that the affected side moved normally on respiration, but that movement on excursion was 1 cm. while that of the unaffected side was 4 cm. It is interesting to note that Greenwald and Kaufman, writing as late as 1928, stated that paradoxical movements occur in hernia and inferred this to be the differentiating point in diagnosis. Botteri [71] found the diaphragm in his case to be immobile. Goriainova spoke of paradoxical movement on deep inspiration as Wellman's sign and stated that a positive Wellman sign gave sufficient grounds in all 3 of his cases for ruling out a diagnosis of diaphragmatic hernia. Blackford and Booth found Wellman's sign present in their case but implied a different interpretation, stating that movement was paradoxical on deep thoracic inspiration but normal on deep abdominal inspiration. Via [72] reported normal but reduced excursion of the diaphragm on the affected side and normal excursion on the other side. Tardieu and Guilbert [73] mentioned that roentgen study in their case suggested eventration, but they did not mention movements of the leaflets of the diaphragm.

The cardiac shadow was invariably greater than normal in the right side of the chest in cases of eventration on the left side and was usually unchanged in cases of eventration on the right side. This observation is relatively constant both in cases of eventration and in cases of hernia and therefore offers no point in differentiation. In cases of eventration on the left side this change in the cardiac shadow to the right has many times been called dextrocardia. It is, however, not true dextrocardia. In cases of eventration the diaphragm is displaced superiorly, causing the heart not to be displaced to the right but rather to be pushed to the anterior thoracic wall with the end-result total displacement of the heart upward, rotation and elevation of the apex and curving of the aorta with broadening of the aortic shadow. The heart assumes the shape of an egg according to Dillon and becomes more and more aortic in form.

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70. Ottosen: Hospitalstid. **67**:465 (July 23) 1924.

71. Botteri: Gior. di clin. med. **11**:1045 (Oct.) 1930.

72. Via: J. de radiol. et d'électrol. **16**:590 (Oct.) 1932.

73. Tardieu and Guilbert: Bull. et mém. de la Soc. de méd. de Paris **9**:310, 1931.

Other interesting associated roentgenologic observations have been reported. An esophagotracheal fistula in Lerche's case, hour-glass stomach in Verbrycke's fifth case and mild elevation or rudimentary eventration in Dillon's case add interest to the subject.

It has been reported several times that on inspiration the entire mediastinum moves to the side opposite the one affected. This was noted in 1 of our cases.

ELECTROCARDIOGRAPHIC OBSERVATIONS

A number of reports have been made regarding the electrocardiographic observations in cases of eventration. This study was undoubtedly done because of apparent dextrocardia. Baetge [74] probably made the first studies in 1913 and found certain departures from normal, but these have not been confirmed by subsequent reports. He stated that in lead 1 there was a negative Q wave which is not present in the normal electrocardiographic tracing. The P wave was shorter than normal but was not convergent, while the T wave was diphasic. In lead 2 the diphasic fluctuation was more pronounced, with first a negative, then a positive, wave. The greatest anomaly, according to Baetge's early study, appeared in lead 3. The T wave was again diphasic, the P wave was negative, and the Q and S waves were not pronounced. The R wave was lower and double-notched.

Siebeck [75] in discussing the heart in association with relaxed diaphragm mentioned the slowing of the heart and extrasystole, an observation which was confirmed by Labbé. Heudtlass, Maggi and Garre [76] after an electrocardiographic study reported sinus arrhythmia. Auricular fibrillation was present in 1 of our cases, but we feel that it was coincidental and not a result of eventration. Maher and Blackwood [77] in 1 case, Wood and Wood in 2 cases, Blackford and Booth in 1 case and Jewett in 1 case noted normal electrocardiographic tracings.

OTHER OBSERVATIONS

Korns in his résumé called particular attention to a sign based on the physiology of the diaphragm and cited the article by Hoover,[78]

74. Baetge: Deutsches Arch. f. klin. Med. **110**:49 (March) 1913.

75. Siebeck: München. med. Wchnschr. **79**:265, 1931.

76. Heudtlass, A. P.; Maggi, A., and Garre, O.: Prensa méd. argent. **20**:461 (March) 1933.

77. Maher, P. P., and Blackwood, J. D., Jr.: U. S. Nav. M. Bull. **30**:359 (July) 1932.

78. Hoover, C. F.: Functions of the Diaphragm and Their Diagnostic Significance, Arch. Int. Med. **12**:214 (Aug.) 1913; Diagnostic Signs from the Scaleni, Intercostal Muscles and the Diaphragm in Lung Ventilation, ibid. **20**:701 (Nov.) 1917; Functions of Intercostal Muscles, J. A. M. A. **73**:17 (July 5) 1919; Am. J. M. Sc. **159**:633 (May) 1920.

whose work on the diaphragm brought added knowledge of the function of this organ. In brief, he stated that unopposed by phrenic action the intercostal muscle will cause the entire costal margin to move away from the midline and that unopposed by the intercostal muscles the diaphragm will draw the entire margin toward the midline. The more nearly the curve of all or any part of the diaphragm approximates a plane, the greater mechanical advantage will that part of the diaphragm have in control of the costal margin to which it is attached. Therefore, the movement of the costal borders is a reliable index of elevation or depression of the diaphragm. The diaphragm and intercostal muscles are therefore antagonists. Normally the intercostal muscles are the stronger, and therefore on inspiration the costal margins throughout their whole extent move away from the midline. Korns made use of these facts and applied them to advantage in making a clinical diagnosis of eventration and in differentiating it from hernia. He stated that if one half of the diaphragm becomes accentuated without the formation of synechia between the thoracic wall and the phrenic leaf the result is an increase in the disparity between the resultant line of traction of the diaphragm and the curve of the diaphragm, and inspiratory divergence of the costal margin from the midline will be considerably in excess of that of the opposite normal side. Korns' remarks on this sign led Lord in 1927 to urge the use of these observations. Uspensky noted this observation in 4 of 5 cases and spoke of the phenomenon as Korns' sign.

Schlippe's procedure for measuring intragastric pressure has been mentioned by various authors. By inserting into the stomach a rubber tube to which is attached a rubber balloon which is blown up after the tube is in place and by connecting the space end with a measuring manometer and chest straps for simultaneously recording inspiration and expiration the relation between these and intragastric pressure can be observed and recorded. Normally intragastric pressure on an intact diaphragm would be increased on inspiration and decreased on expiration by pressure on the diaphragm from above. This relationship is maintained in cases of eventration of the diaphragm, but in cases of hernia of the diaphragm, in which the stomach invades the thorax through an opening in the leaf, no such pressure would be exercised and the reverse condition would be obtained. While in our first case this test was applied with the results that theoretically should be observed, many authors have condemned the method—some without using it in the conduct of their own cases.

The electric stimulation of the phrenic nerve has been suggested, and observation under the fluoroscope as to the extent of the excursion of the diaphragm has been carried out. Theoretically, if this test is applied to a normal person in the interim between respirations when other influencing factors of respiration are eliminated, it should result in a degree

of excursion directly proportional to the strength of the stimulus and the amount of normal conducting tissue in the phrenic nerve. If the phrenic nerve is paralyzed no resulting contraction takes place. Practically, reports in the literature indicate that this test is useless, as collateral stimulation of other muscles, like the scalene and intercostal muscles, and isolated effects on the diaphragm are by no means certain.

Pneumoperitoneum with subsequent fluoroscopy has been mentioned by many authors but the majority have felt that it is attended with danger, especially if done in the presence of a hernia of the diaphragm when air might enter the pleural cavity. Lord stated that it is not justified and mentioned gangrene of the stomach as a complication to the procedure. Overholt [79] agreed that it should not be done. Many authors mentioned it as a diagnostic procedure, but none seem to have attempted its use. Walton, for example, suggested pneumoperitoneum as the only diagnostic sign of any pathognomonic value, but he did not employ it in the study of his case. We gather from a study of the literature that this procedure has been a measure to write about but not to perform and, therefore, conclude that it should be eliminated from the modern diagnostic armamentarium. Dillon stated that Goetze and Schlecht and Wels recommended the procedure and that Freud and Horner in applying the method did not obtain satisfactory results because of adhesions in the abdominal cavity. In the case of Schlecht and Wels perforation of a gastric ulcer developed twenty-one days after pneumoperitoneum, and the patient died twenty-four hours after an operation.

DIAGNOSIS

It becomes evident from the foregoing material that a clinical diagnosis of eventration of the diaphragm even with the aid of all the available measures of precision is most difficult. Diagnosis from the physical signs is impossible, although Bayne-Jones stated that Janeway made a diagnosis on these signs alone. He further stated that this was the first instance of intravitam diagnosis of the condition. One might suspect hernia, eventration or pneumothorax from the physical signs, but if the sign mentioned by Korns were constant one might definitely diagnose the condition. It is interesting to note that Kunkel [80] in presenting his case, the reproduced plates of which are very indistinct, said that "the combination of physical signs encountered is apparently pathognomonic of the pathology and if kept in mind similar cases may be recognized and properly certified to in many instances where X-Ray or post-mortem examination is not possible." This is somewhat contrary to the general thought, but on the other hand Dillon said that he was able to make a

79. Overholt, R. H.: Ann. Surg. **91**:381 (March) 1930.

80. Kunkel, W. M.: Pennsylvania M. J. **33**:63 (Nov.) 1929.

correct diagnosis by clinical examination in 2 cases and that the diagnosis was later confirmed by fluoroscopic examination. Bamber suggested that in his case the condition should have been diagnosed "from the long history and the gurgling sounds so plainly heard in the chest posteriorly." To make a positive diagnosis on physical signs necessitates pathognomonic signs, and as there are none, in our opinion, one can only suspect the presence of eventration. Eggers said that he made a diagnosis of eventration after roentgenologic examination; the surgical preoperative diagnosis based on symptoms was hernia, the operative diagnosis was hernia and postmortem examination revealed localized eventration of the diaphragm. When such difficulties exist one must hesitate to make a positive diagnosis from physical and clinical signs alone.

A differential diagnosis of eventration must be made from hernia of the diaphragm, pleurisy with fluid, thickened pleura, thoracic stomach, pulmonary cysts, pulmonary tumors, atelectasis, emphysema and neurosis.

A differential diagnosis though at times fraught with difficulties is important whenever possible. Needless surgical procedures have not infrequently resulted from mistaken diagnosis. Exploratory thoracentesis and thoracotomy have been performed several times for fluid when eventration existed instead. Clopton's [60] case was a striking example of this fault in diagnosis. He reported the case of a baby 14 months old in whom a part of the eighth rib on the left side was removed and a tube was inserted for drainage. At the time the child had influenza and bronchopneumonia, followed by what was thought to be empyema. The drain remained in for six months, and a week after it was removed an abscess formed along the tract anterior to the fifth rib. When the child came under Clopton's observation the temperature was high, thirst was violent and vomiting was continuous. On the first roentgen study it was thought that diaphragmatic hernia existed, but later a diagnosis of eventration was made. Reexamination of the films taken at the time of the resection of the rib revealed the same condition. In Allan's case puncture was performed to drain off fluid. Levine mentioned that the stomach may be punctured by thoracentesis if eventration is mistaken for fluid. Thompson concluded in his case that pleural effusion existed and that the chest should be punctured, but the patient refused permission, and subsequent examination proved the objection a wise one as eventration was found. Morrison made a tentative diagnosis of pleural thickening in 1 of his cases, while Fatou and his associates suspected pleurisy at the first examination. Yater and Rodis [81] reported a case of pleural effusion in which eventration was suggested on roentgen study of the

81. Yater, W. M., and Rodis, I.: Am. J. Roentgenol. **29**:813 (June) 1933.

patient in a standing position, but this impression was readily cleared away when roentgen examination was made with the patient in the recumbent position.

Probably of all diseases from which eventration must be differentiated, hernia of the diaphragm is seen most frequently. The history of acute onset of symptoms following trauma leads some to favor the diagnosis of hernia. Others feel that the fluoroscopic study is all that is necessary for differentiation, but the two conditions remain at times difficult or impossible to differentiate.

Goodall and Hoyt [82] in a recent study and report on thoracic stomach present another differential problem which, while no such case has come under our observation, makes one feel that the roentgen study is readily and completely clarifying.

Levin and Cunningham and Shaw [83] and others have mentioned that eventration might incorrectly suggest a neurosis and that patients have symptoms resembling those of a neurotic person. We readily appreciate this, particularly when one reviews the detailed histories of some of the cases found in the literature. As in our first case, symptoms were bizarre and no clue was definitely suggested until after fluoroscopic study, although pleural effusion was considered after physical examination.

Exploratory operation has been suggested in preference to pneumoperitoneum, and while the latter is to be condemned, the former is a radical step to take to make a diagnosis and hardly seems justifiable.

In summary, the diagnosis of eventration of the diaphragm is difficult and rests with no one procedure unless Korns' application of the physiologic studies of the diaphragm becomes a universal sign.

PROGNOSIS

The prognosis of eventration is difficult to make and must therefore be guarded. In general, as far as life is concerned it is usually good, but it is, however, a disabling disease in many persons. In those cases in which there is true eventration, that is, congenital displacement, if severe symptoms do not arise in the first five years of life they usually do not make their appearance until the fourth decade or even much later. Quénu and Fatou felt that the benignity of eventration is exaggerated and that such patients are subject to more symptoms and complications than those with hernia of the diaphragm. Blackford and Booth, quoting a personal communication from R. Bartholomew, stated that the latter had a patient who was several months pregnant in whom elevation of

82. Goodall, H. W., and Hoyt, L. H.: Thoracic Stomach, Arch. Int. Med. **53:** 549 (April) 1934.

83. Cunningham, L. W., and Shaw, W. M.: J. Florida M. A. **11:**7 (July) 1924.

the left side of the diaphragm was noted. Labor was precipitated, resulting in complete rupture of the diaphragm. It was concluded from this that eventration is a menace to young women of the child-bearing age.

TREATMENT

Medical management is the treatment of choice. Such therapy must inevitably be meager and entirely symptomatic. Wood and Wood tersely summarized management by saying that no curative treatment is possible. Absolute rest is essential, and while this may not necessarily be rest in bed, absence of physical exertion is essential. The relief of gastro-intestinal symptoms such as gas, bloating, fulness, nausea and vomiting, which are often distressing, is urgent. The use of the usual intestinal antispasmodics and a bland, nonirritating diet with a low residue may at times add to the comfort of the patient. Lord in the report of his first case stated that rest in bed always improved this particular patient. Many patients were found to be overweight, a condition which should be corrected. Sedatives are at times imperative, and we believe that bromides in amounts sufficient to produce physiologic effects are of much value, while the barbiturates are the next choice, and only occasionally are morphine and allied drugs resorted to for relief of distress. The treatment of associated diseases is not to be overlooked or neglected. Dillon's exhaustive study on the subject contained but a few lines on therapy and in summary said that hygienic and dietetic measures are the only reliable means of relief.

Surgical intervention in cases of eventration has been done a number of times but has not proved to be a marked success. Quénu and Fatou in a splendid report said that in all literature one finds the statement that hernia is operable and eventration is not, and they determined to disprove this idea. Careful search of the literature on the subject of surgical intervention in the presence of eventration may be summarized in the following outline:

	No. of Cases
Operations directly on the diaphragm for cure or relief	4
Exploratory operations	14
Operations for the coexisting disease	14

Operations on the Diaphragm.—This means surgical procedures on the diaphragm with the intention of correcting the pathologic condition present.

1. Lerche, through an abdominal incision, plicated the diaphragm in a woman, aged 38, who had also an esophagotracheal fistula. He made a final report [84] with

84. Lerche, W.: Infected Mediastinal Lymph Nodes as Source of Mediastinitis, Arch. Surg. **14**:285 (Jan., pt. 2) 1927.

necropsy observations five years after the original operation. There was no trace of the phrenoplication; the affected leaf had been held in its place since the operation, and the patient had thereby been relieved of distressing symptoms.

2. Fatou and Lafourcade [85] reported a case in 1922 which Fatou again reported in 1928 [30] in which a man 44 years old complaining of gastric distress with emaciation was operated on through an abdominal incision. All the organs under the diaphragm were pulled down, the spleen was removed and the incision was closed. Immediately a thoracic incision in the seventh interspace was made, the ribs were separated and plication of the diaphragm from above was done. Three days later the patient died. Necropsy revealed that the plication had not held.

3. In Morrison's case a girl aged 10 was operated on by the thoracic route only. The diaphragm was found to be thinned out and of dense fibrous tissue. Partial excision of the diaphragmatic sac was done, followed by an uneventful convalescence. An examination three years later revealed the "bowline" not as high as before, the movements of the diaphragm free but reversed and no symptoms.

4. Quénu and Fatou reported their case in which a pneumothorax was done first, with a second stage consisting of a thoracolaparotomy beginning in the sixth interspace with resection of the costal cartilage. One hand was introduced, and the abdominal organs were pulled down. The diaphragm was then plicated on its convex surface. Roentgenographic study after the operation revealed the diaphragm 8 inches (5.08 cm.) lower, and two and one-half months later there were no symptoms.

Exploratory Operations Not Directly on Diaphragm.—1. Fischer in 1914 did a thoracotomy on a patient convalescing from pneumonia and typhoid fever, but finally made a diagnosis of eventration. The authenticity of the diagnosis of this case was questioned by Korns.

2. Bouquet, Masselot and Jaubert de Beaujeu in 1921 made a diagnosis of diaphragmatic hernia. Thoracotomy revealed no hernia; at necropsy eventration was found.

3. In Clopton's case, which was mentioned previously, thoracotomy and resection of a rib was done because eventration was mistaken for pleural effusion.

4. Glaser's patient was operated on by Korte in 1903. An exploratory laparotomy was done for hernia, but eventration was found. The abdomen was closed with no further surgical procedure.

5. Roux in 1915 made a preoperative diagnosis of hernia of the diaphragm, but eventration was found on exploratory operation, so no further surgical steps were taken.

6. Schlecht and Wels [86] confirmed their diagnosis by exploratory operation, but no corrective procedure was attempted.

7. Robineau and Quénu in 1919 performed a thoracolaparotomy on a patient of Louste and Fatou. The preoperative diagnosis was hernia of the diaphragm, but pleuroperitoneal tuberculosis with caseous masses was found at operation. The wound was immediately closed; necropsy disclosed eventration.

8. Bayne-Jones' patient was operated on by Phinney for disease of the gallbladder. On exploration the gallbladder was found to be normal, but eventration

85. Fatou and Lafourcade: Bull. et mém. Soc. méd. d. hôp. de Paris **46**:505, 1922.

86. Schlecht and Wels: Fortschr. a. d. Geb. d. Röntgenstrahlen **27**:544, 1920.

of the right side of the diaphragm was disclosed, for which nothing was done. The patient died ten days later.

9. Verbrycke's first patient was operated on by C. S. White in 1914. The colon was freed, but no further repair was attempted. Three years later the symptoms were improved.

10. Madinaveitra [87] reported the case of a patient who was operated on for cancer of the stomach which did not exist; eventration was found, but no further surgical intervention was done.

11. Jawara and Dumitresco-Mante did an exploratory laparotomy subsequent to puncture of the base of the right lung at which time fluid was obtained. A hydatid cyst was found under an elevated diaphragm. Two years later the patient was well.

12. In Egger's case a preoperative diagnosis of hernia of the diaphragm was made. A simple laparotomy was done with no repair of the diaphragm. The child died fourteen hours after the operation; necropsy revealed eventration.

13. Heidenreich [87] reported a case in which an exploratory laparotomy was done and a gastric volvulus and eventration were found.

14. Our first case, which is reported later, falls into this group.

Operation for Coexisting or Associated Disease.—1. Baetge's case in 1913 was one of cholelithiasis in a man aged 28. Eventration of the diaphragm was found on operation.

2. Sicilliano reported a case of pyloric obstruction due to cancer. At operation this condition was confirmed and eventration was found. A gastro-enterostomy was done.

3. Kienböck's [88] patient was operated on to relieve an obstruction of the pylorus due to ulcer, at which time the diagnosis of eventration was confirmed.

4, 5 and 6. Boughert (de Lyon), cited by Quénu and Fatou,[29] operated on 3 patients with ulcer on the lesser curvature of the stomach coexisting with eventration. In 1 a partial gastrectomy was done, in 1, a Balfour operation with a gastro-enterostomy four months later, and in 1, a gastro-enterostomy.

7. Berg in 1917 resected 3 feet (91.4 cm.) of colon in a case of megacolon associated with eventration on the right side. This was the case of Aronson,[89] of which Korns said that if eventration was confirmed at operation "the author's vague description of the findings raises much doubt."

8. Quénu cited the case of Carnot in which a total colectomy was done for the relief of megacolon. Eventration of the diaphragm was found, but no direct attack was made on this pathologic condition. The patient died the next day.

9. Wood and Wood reported the case of a man 68 years of age whose health had been good, and he had worked for forty-five years without losing a day. An intestinal obstruction developed. About one week after the operation a high diaphragm was noted.

10. Verbrycke's second patient was operated on for perforated gastric ulcer high on the lesser curvature of the stomach, at which time many adhesions and an eventration of the diaphragm were found. Verbrycke stated that three weeks later

87. Heidenreich: Prensa méd. argent. **19**:792 (Oct.) 1932.

88. Kienböck: Fortschr. a. d. Geb. d. Röntgenstrahlen **21**:322, 1914.

89. Aronson, E. A.: New York M. J. **108**:196, 1918; M. Rec. **93**:37, 1918.

the stomach was functioning normally and the diaphragm was somewhat lower. Roentgenograms taken four months later showed the diaphragm to be 4 inches (121.9 cm.) lower. This and the first case that this author reported seem to be the only 2 on record in which the position of the diaphragm was improved by the correction of associated conditions, as confirmed by roentgen study.

11. In Morrison's case the patient was operated on for pyloric obstruction due to torsion of the stomach, at which time eventration was found.

12. Golob's patient showed a "growth at the cardia" on esophagoscopic examination. Lilienthal performed this operation and found a carcinoma at the cardiac end of the stomach and the right side of the diaphragm elevated high in the chest.

13. Foster's patient was a girl aged 14 years who had previously been healthy and now complained of pain in the lower portion of the abdomen. At operation a large ovarian cyst was found and removed. A search for the appendix disclosed an abnormal position of the transverse colon. Subsequent roentgen study revealed a high diaphragm and the cecum above the liver.

14. In Allan's case puncture was done for the treatment of pleural effusion on the left side, which was not present. Eventration was found on subsequent study.

This review of surgical management of eventration or surgical intervention in associated conditions leaves one with the impression that such treatment offers little hope for a cure.

REPORT OF CASES

CASE 1.—*History.*—B. T. H., a fireman, was a married man aged 45, the father of two children. His chief complaint was choking spells and fainting with shortness of breath and pain in the lower anterior part of chest.

The onset of the symptoms was rather gradual, although the patient dated their beginning from an accident (this accident was believed to have been preconceived to gain compensation). However, the symptoms had been present for about nine years. The patient met with an accident in October 1924 when he was thrown from a fire-truck, striking the lower anterior part of the chest against an object and being rendered semiconscious. He likewise sustained a fracture of the left humerus and left wrist. The first symptoms noted were an ache in the left upper extremity extending into the back of the neck and numbness of the fourth and fifth fingers of the left hand which appeared white when the patient arose in the morning and were so stiff that he could barely move them. Since that time he had had an attack of weakness two and three times a day. These attacks consisted of cold sweats, weakness in the knees, sensation of cold and warmth, gasping for breath and the impression that consciousness was leaving him. He felt that there was pressure against the heart. Dyspnea appeared after the accident and had gradually grown worse, being exaggerated on exertion, with palpitation of the heart. The cough which occurred with attacks of dyspnea was unproductive. There was pain in the lower anterior portion of the chest on the left on deep breathing, exertion or emotional excitement. Nervousness was apparent.

Family History: The patient's father died at the age of 64 of an unknown cause. The mother, aged 69, two brothers, aged 52 and 37, and four sisters aged 50, 48, 40 and 38, respectively, were living and well. No chronic diseases were known to have existed in the family. Three sisters died in infancy.

Previous Personal History: No childhood diseases were known. The patient had an occasional cold. His tonsils were removed in 1913. He had had no major

illness up to the time of the accident. In the previous twelve years the official record of the department in which he worked showed only minor illness such as cough, grip and minor infections; there was no special mention of severe symptoms suggesting thoracic or gastro-intestinal disease.

Physical Examination.—The pulse was 92, the temperature, 98 F., the respiratory rate, 24, and the blood pressure, 144 systolic and 90 diastolic. The pulse was irregular in rhythm and volume. Many teeth were missing; the remainder appeared normal. The tongue was clean. The tonsils had been removed. The gag reflex was increased. The pupils reacted to light and in accommodation. The thyroid gland was normal. There was no general adenopathy. The nasal accessory sinuses and the mastoid were clear.

The chest was of the asthenic type. Expansion was free and apparently equal. The right lung was apparently normal. On the left side anteriorly there was a tympanitic note from the fourth rib distally. Laterally and posteriorly in the

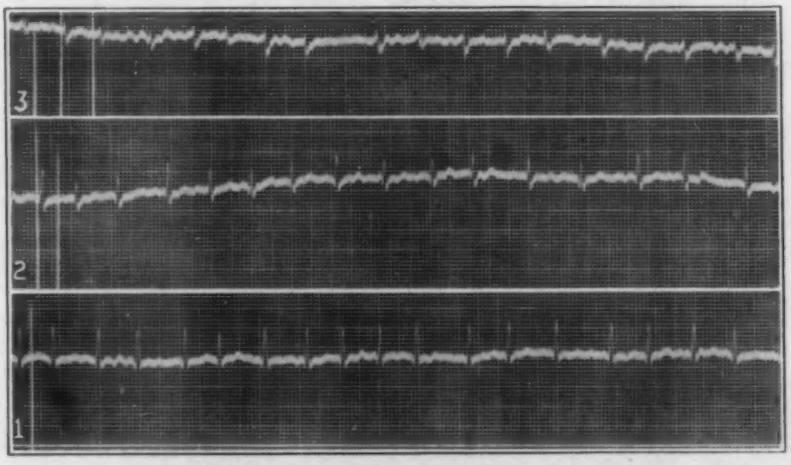

Fig. 1 (case 1).—The electrocardiographic tracing which confirmed the impression of auricular fibrillation with myocardial damage.

axillary line was an area of dulness from the angle of the scapula down to the base of the lung. Anteriorly there was a gastric tinkle over the fifth interspace. Over the entire left lung in the lower half anteriorly and posteriorly were diminished breath sounds and voice sounds. No râles were noted. Examination for Hoover's or Korns' observation was made after roentgen examination. Measurements of the chest movements including those of the subcostal angle were not indicative of any difference in the two sides, although the patient was rather obese and accurate measurements might not have been obtainable. Examination of the heart revealed that the apex was not visible or palpable. There was no bulging of the precordium and no thrills. The left border extended 9 cm. to the left of the midsternal line in the fifth interspace and 6.5 cm. to the right of the midsternal line. There was a definite disorderly irregularity suggesting auricular fibrillation. The heart sounds were of poor quality and intensity. The apex beat was faster than that of the pulse.

The abdomen was well rounded with considerable subcutaneous fat. The liver, spleen and kidneys were apparently normal. There was no local or general tenderness or rigidity and no masses. All the superficial and deep reflexes were normal. The extremities were normal. Urinalysis gave normal results.

Examination of the Blood.—The white cell count was 9,150, the red cell count was 5,000,000, and the hemoglobin content was 93 per cent. The differential count was: band forms, 3 per cent; segmented forms, 63 per cent; eosinophils, 2 per cent; monocytes, 2 per cent, and large and small lymphocytes, 31 per cent.

Electrocardiographic Study.—The ventricular rate was 140 with irregular rhythm. The P wave was replaced by fibrillary waves. The Q R S complex occupied 0.08 second and was upright and slurred in leads 1 and 2, inverted and

Fig. 2 (case 1).—A roentgenogram of the chest showing the curved unbroken bowline with the air-filled stomach below.

split in lead 3 and of low voltage throughout. The T wave appeared to be inverted in lead 1 and upright in leads 2 and 3; they were of low voltage throughout. The diagnosis was auricular fibrillation with myocardial damage.

Roentgen Study.—Several examinations were made in a short period of time by different roentgenologists.

The first examination was made by Dr. A. B. Moore and Dr. E. M. McPeak. Fluoroscopic examination of the chest revealed marked elevation of the diaphragm on the left. Examination of the esophagus and stomach revealed the stomach high on the left side although apparently below the diaphragm. The roentgenologist believed that this was the result of eventration of the diaphragm, although the possibility of hernia could not be entirely excluded. Apparently the colon was very high on the left side. Further examination was made a week later. The

ribs on the left side showed no definite evidence of injury. The diaphragm was markedly elevated. The stomach was situated high on the left side but was definitely beneath the dome of the diaphragm.

The second examination was made about two weeks later by Dr. Claude Moore who made the following report: The patient was examined under the fluoroscope in the sitting position because he was too weak to stand. There was marked elevation of the diaphragm on the left side with decrease in the chest space on the left and compensatory dilatation of the right side of the chest. There was rather extreme motion of the diaphragm on the right. The heart was displaced to the right so that the center of the heart was about in the midline. The diaphragm on the left was fixed and reached to the level of the third interspace anteriorly

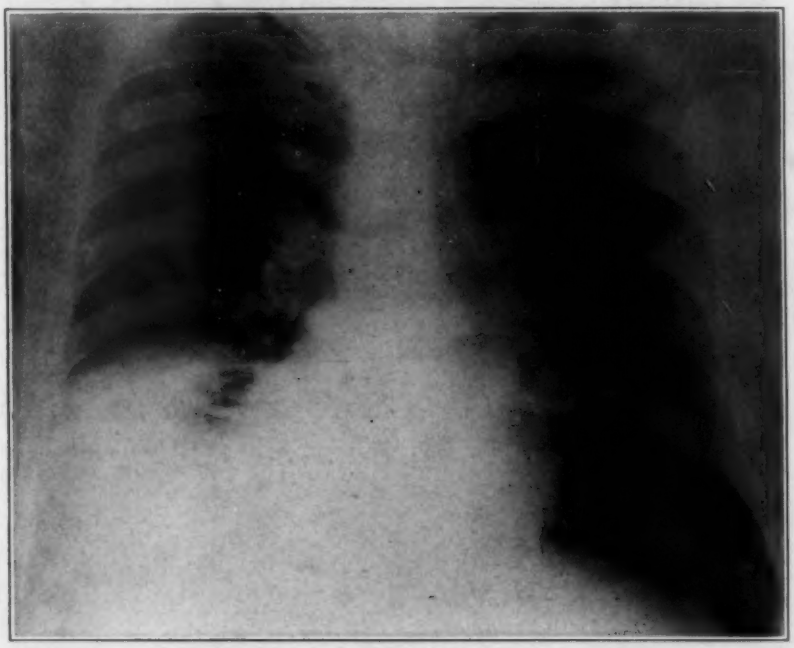

Fig. 3 (case 1).—A roentgenogram showing the high diaphragm and the stomach below apparently filled with fluid.

and to the level of the seventh interspace posteriorly. Respiratory motion showed paradoxical motion of the diaphragm on the left. In other words, as the diaphragm went down on the right side it went up on the left side, and the mediastinum was pulled to the right. There was considerable gas in the stomach, and the left border of the heart could be seen through the gas. The upper walls of the stomach and diaphragm on the left side were from two to three times average normal thickness. The impression was that the condition was the result of an old respiratory process, either of inflammation or of injury. If it were the result of a congenital condition or of paralysis of the left phrenic nerve the diaphragm would have been markedly thinned out. The diagnosis was marked elevation of the diaphragm on the left side with paradoxical motion on respiration.

Operation and Surgical Notes.—A Mayo-Robson incision on the left side permitted exploration of the abdomen and the left side of the thoracic cavity. The

diaphragm on the left was tense and at the height of the fourth rib. The stomach, large and small intestine, omentum and spleen were in the thoracic space. The viscera were dislodged with difficulty and placed in the abdominal cavity, and the wound was closed.

Exploration revealed the following: 1. The diaphragm was displaced to the level of the fourth rib and was tense at all times during both inspiration and expiration. 2. The mediastinum containing the heart was bulging into the cavity of the chest. The diaphragm was so thin as not to be recognized, and the impression was that the heart was exposed and covered only by the pericardium. 3. The ribs surrounding the wall of the chest were superficial, with the thinnest possible covering that could hardly be recognized as tissue of the diaphragm. 4. Over the anterior lower border of the chest was a curtain of tissue suggestive of a former diaphragmatic attachment.

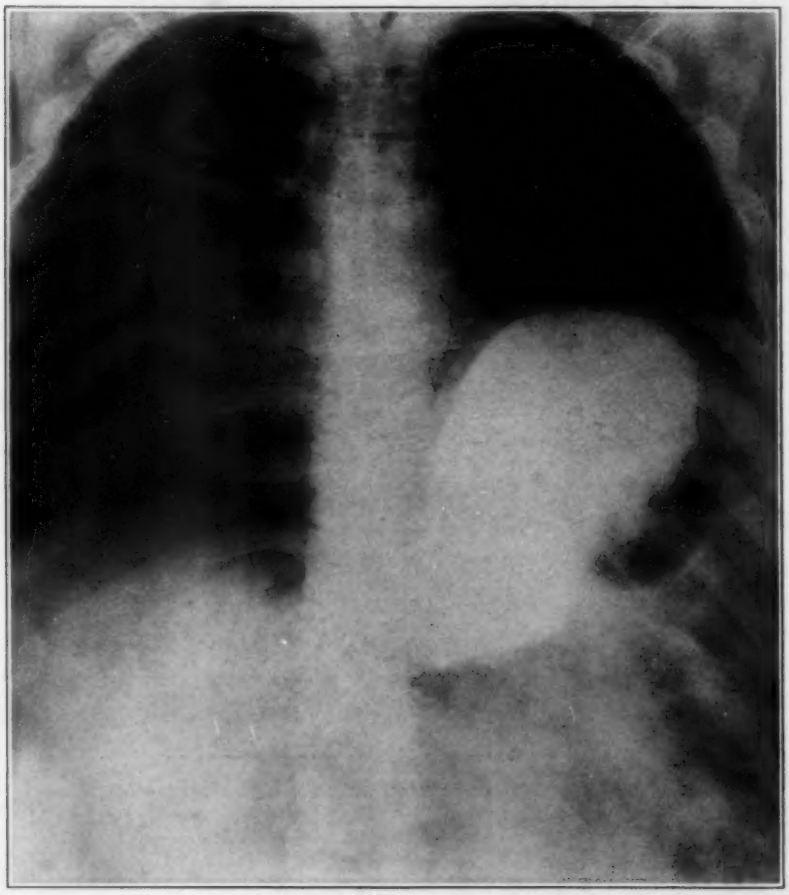

Fig. 4 (case 1).—A roentgenogram of the stomach filled with barium below the elevated diaphragm. The heart shadow is to the right.

The opinion was that in order to repair the diaphragmatic defect it would have been necessary to open the wall of the chest anteriorly up to the third rib. Having accomplished this it did not appear possible or plausible to place stitches that would hold in the presence of a thinned out lateral diaphragmatic wall. It seemed unjustifiable to subject the patient to grave risk with little hope of accomplishing any good.

CASE 2.—*History.*—E. H. H., a married man aged 42, a policeman, was shot accidentally while cleaning a pistol. The bullet pierced the anterior wall of the chest to the left of, and just below, the left nipple and made its exit posteriorly

Fig. 5 (case 1).—A lateral view showing the high diaphragm and the stomach filled with barium.

immediately below the angle of the scapula. He was taken immediately to the emergency room of the Garfield Memorial Hospital. The pulse was weak and rapid, and the patient was in a state of severe shock. Morphine sulphate was given subcutaneously with physiologic solution of sodium chloride. The patient remained in the hospital eighteen days, and then was taken home in an ambulance. He returned to work about two months later, apparently cured. Physical examination during his stay in the hospital revealed a normal condition with the following exceptions: The blood pressure on admission was 48 systolic and 32 diastolic, rising to 80 systolic and 70 diastolic in the course of six hours after emergency treatment. There was evidence of anemia and shock, and a few scattered bubbling

râles were heard over the anterior lower portion of the chest on the left near the site of the wound. Two days later effusion of the left pleural cavity developed. There were some coughing of blood and pain in the chest with nausea, restlessness and fever until the patient was discharged. The diagnosis was gunshot wound of the chest with injury to the pericardium and subsequent pleural effusion. Two and one-half months later a fluoroscopic examination revealed the diaphragm on the left to be quite high and a large gas bubble of the stomach immediately below. At this time we were unable to determine definitely whether the shadow was of the diaphragm or of a possible fluid level. Subsequently a roentgen examination was made.

The previous and familial history was irrelevant.

Physical Examination.—The blood pressure was 120 systolic and 80 diastolic. The heart gave no evidence of displacement, enlargement, murmurs or arrhythmia.

Fig. 6 (case 2).—A roentgenogram of the chest showing the curved, unbroken bowline with the air-filled stomach. Thickening of the interlobar pleura is evident.

The sounds were slightly distant. The right lung was normal in every respect both anteriorly and posteriorly. Percussion over the left lung revealed diminished sounds not heard in the lower third of the chest anteriorly and posteriorly. There were diminished breath sounds on the left over the dull area but no râles. No gastric tinkle or gurgle was heard, and there was no tympanitic note over the anterior lower portion of the chest on the left. There seemed to be a lag on the left side. There was no Korns' sign. The remainder of the physical examination gave normal results.

Roentgen Examination.—Examination on the day of admission to the hospital revealed complete opacity of the entire left side of the chest with displacement of the heart and great vessels to the right. The trachea was also markedly displaced to the right. The opacity was evidently due to hemorrhage.

Examination on the fifth day of hospitalization revealed opacity of the entire left side of the chest with displacement of the heart and great vessels to the right. The opacity appeared to be caused by fluid.

Fluoroscopic examination in the upright position on the eighth day of hospitalization revealed no evidence of pneumothorax. Uniform opacity of the entire left side of the chest suggested the presence of fluid.

Examination on the day of discharge revealed the exudate in the left side of the chest to be materially decreased over the previous examinations. The upper third of the left lung was pneumatic.

Examination was made six weeks after discharge from the hospital. Posteriorly and anteriorly the chest showed evidence of an irregular area of increased density in the region of the base of the left lung where there was also suggestive evidence of some insistent air. The observations were compatible with a diagnosis of

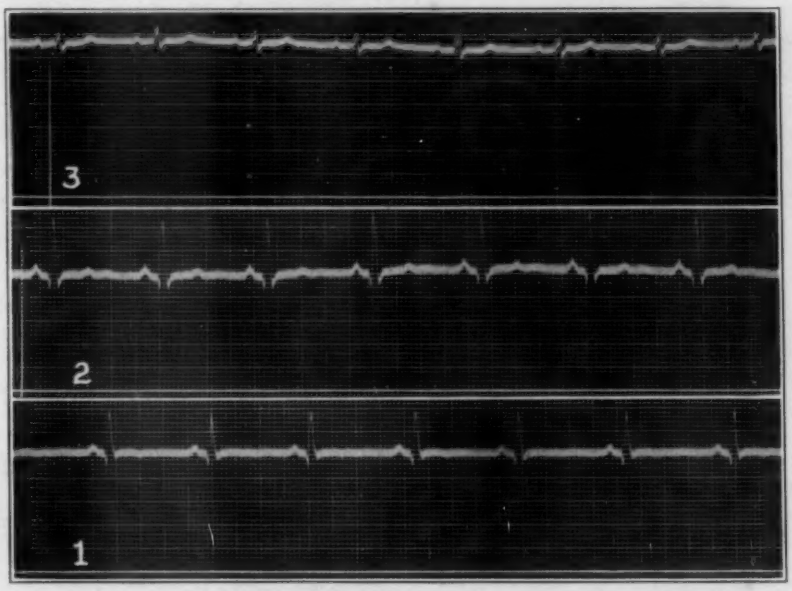

Fig. 7 (case 2).—The electrocardiographic tracing which confirmed the impression of myocardial damage.

pleural effusion of moderate degree with a small pneumothorax and some pneumonitis, but the possibility of herniation of the diaphragm was considered. A fluoroscopic examination was recommended. The apex of the left lung and the entire right lung were relatively clear. The heart was of normal size and shape but was displaced slightly to the right.

Examination by another roentgenologist ten weeks after discharge from the hospital revealed a rather marked elevation of the diaphragm on the left with thickening of the pleura over it. Fluoroscopically there was no evidence of movement of the diaphragm on this side. The diaphragm on the right side appeared to be normal.

Electrocardiographic Study.—The conclusion was that there was evidence of mild myocardial damage.

Summary.—The patient had a gunshot wound of left side of the chest with subsequent pleural effusion. The effusion cleared up, and later eventration of the diaphragm was found, probably caused by injury or section of the phrenic nerve.

SUMMARY

A complete résumé of eventration of the diaphragm was given with a study of the literature and the addition of 2 new cases.

ACUTE APPENDICITIS IN DOGS

AN EXPERIMENTAL STUDY

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AND

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Stimulated by a desire to compare the conservative and operative methods of treating acute appendicitis, we undertook to produce acute appendicitis in dogs.

Anatomically the dog has no appendix, but the cecum, which is blind, serves as an admirable substitute. The terminal portion of the ileum joins the cecum at its junction with the ascending colon. The lesion of acute appendicitis was produced in varying degrees of severity by ligation of one, two or three of the arterial branches supplying the organ, by crushing and ligating the base of the organ or by a combination of these methods.

EXPERIMENTAL METHODS

Table 1 shows the general plan of the experiment. Appendical damage of mild, moderate or severe degree was produced, and the dogs which survived were examined at intervals thereafter of one, two or three months. Essentially equal numbers of dogs with each degree of damage were examined after operative or conservative treatment. Of the forty-eight dogs in the series twenty-eight survived, fifteen of which were given conservative treatment while thirteen were operated on. The mortality among the dogs with mild appendical damage was 12.5 per cent; among those with moderate damage, 52 per cent, and among those with severe damage, 80 per cent, the total average mortality being 42 per cent.

Conservative treatment after laparotomy to produce the lesion consisted of the daily administration subcutaneously of physiologic solution of sodium chloride and intravenously of a solution of 5 per cent dextrose, usually in doses of 500 and 200 cc., respectively. Morphine was given freely to keep the dogs quiet.

Nothing was given by mouth, and the parenteral fluids were administered until the animal showed a desire for water. The diet was then gradually increased according to the clinical course.

Operative treatment after a laparotomy to produce the lesion began with a second laparotomy from twenty-four to forty-eight hours later. This was done preferably through a second incision (the first operation in the later experiments was through a left rectus and the second operation through a right rectus incision), and drainage of the area around the appendix was instituted with a soft rubber Penrose drain filled with gauze. The inflammatory lesion was disturbed as little as possible, and the drain was sutured in place. The abdomen was closed entirely

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with interrupted stitches in layers. Parenteral fluids were administered as to the animals given conservative treatment. Subsequently reexamination of the dogs was made after one, two or three month intervals, as in the case of those treated conservatively. Table 1, for example, shows that only one of the dogs operated on with severe damage survived. Four other dogs so treated died. The degree of damage was estimated by the measures taken to produce the lesion and careful consideration of the clinical result produced.

RESULTS

Table 2 gives a comparison of the mortality among the dogs treated conservatively and those treated by operation grouped according to the

TABLE 1.—*Summary of Experiment in Twenty-Eight Dogs*

Degree of Damage	Reexamination of 15 Dogs Treated Conservatively			Reexamination of 13 Dogs Treated by Operation			Results		
	1 Mo.	2 mo.	3 mo.	1 mo.	2 mo.	3 mo.	Well	Dead	Mortality, Percentage
Mild.....	2	2	4	2	2	2	14	2	12.5
Moderate...	2	2	3	2	2	2	13	14	52.0
Severe.....	..	..	..	..	..	1	1	4	80.0
Total.....	4	4	7	4	4	5	28	20	42.0

TABLE 2.—*Mortality According to Severity of the Lesion*

Degree of Damage	Number of Dogs	Result		Group Conservatively Treated		Group Operated on	
		Well	Dead	Dead	Mortality, Percentage	Dead	Mortality, Percentage
Mild.....	16	14	2	0	0	2	33.3
Moderate.....	27	13	14	5	42	9	60
Severe.....	5	1	4	1	100*	3	75
Total.....	48	28	20	6	29	14	52

* Only one dog with severe damage was treated conservatively.

severity of the lesion. In the group with mild damage there was no mortality among those which received conservative treatment, but a mortality of 33.3 per cent among those operated on. In the group with moderate damage a mortality of 42 per cent followed conservative treatment and a mortality of 60 per cent followed surgical treatment. In the group with severe damage the mortality was 100 per cent following conservative treatment and 75 per cent following operation. It should be stated that only one animal with severe damage received conservative treatment, whereas four dogs with severe damage were operated on. Total mortality following conservative treatment was 29 per cent and following surgical treatment, 52 per cent. It is only fair to

state that evisceration is more likely to occur in dogs than in man and that this complication caused two of the fourteen deaths following operative treatment.

Fig. 1.—General adhesions after appendictis produced experimentally.

Fig. 2.—Generalized peritonitis in a dog which died after drainage. The drainage tube, drainage tract and generalized peritonitis are shown.

The causes of death are grouped in table 3 which shows 65 per cent of the fatalities to be due to generalized peritonitis. A mortality of 10 per cent was noted in each group with gangrenous appendicitis with

localized abscess, volvulus and evisceration. One dog with gangrenous appendicitis died under anesthesia. The two types of treatment are again compared. The most outstanding finding is a mortality of 23 per cent following conservative treatment of generalized peritonitis in comparison with a mortality of 77 per cent in the group operated on. The total mortality in the series was 30 per cent for the group treated conservatively and 70 per cent for those treated by operation.

Aside from the mortality alone, the observations were of interest because of postoperative conditions, notably adhesions. Table 4 shows

TABLE 3.—*Causes of Death Following Experimental Appendicitis*

Cause	Total		Conservative Treatment		Operative Treatment	
	Number	Percentage	Number	Percentage	Number	Percentage
Generalized peritonitis	13	65	3	23	10	77
Gangrenous appendicitis with localized abscess	2	10	2	100	..	..
Volvulus	2	10	1	50	1	50
Evisceration	2	10	..	..	2	100
Gangrenous appendicitis plus anesthesia	1	5	..	..	1	100
Total	20	100	6	30	14	70

TABLE 4.—*Grade of Adhesions Found Following Experimental Appendicitis*

Degree of Damage	Reexamination of Group Treated Conservatively				Reexamination of Group Operated on			
	1 mo.	2 mo.	3 mo.	Percentage 46.7	1 mo.	2 mo.	3 mo.	Percentage 100
Mild	1, 1*	0, 1	0, 0, 1, 1	63	2, 2	1, 3	2, 3	100
Moderate	1, 1	0, 0	0, 0, 1	43	3, 3	3, 3	3, 3	100
Severe	....	....	....	..	....	....	3	100

* 0 means no adhesions, 1 means mild adhesions, 2 means moderate adhesions and 3 means severe adhesions.

the grade of adhesions found in each of the twenty-eight dogs which survived, grouped according to the degree of appendical damage produced. For example, according to table 4, four dogs with a mild degree of damage which were conservatively treated were reexamined after three months. Two of these showed no adhesions and two more showed mild adhesions. Similarly, of two dogs with mild damage treated by operation and examined again after three months, one dog had moderate adhesions and one, severe adhesions. The striking fact brought out in this table is that less than one half of the dogs treated conservatively had peritoneal adhesions except over the surface of the appendix itself, whereas 100 per cent of those which underwent surgical intervention were found after various intervals to have adhesions. In all

the dogs but one the adhesions were of at least moderate degree, and nine of thirteen dogs showed severe adhesions.

Fig. 3.—Generalized peritonitis in a dog which died, showing the cavity of an appendical abscess.

Fig. 4.—A single fine adhesion from the omentum to the under surface of the abdominal scar. The appendix and peritoneum elsewhere were entirely without adhesions.

While we realize that human beings and dogs are different, there are certain features which are similar. Infection, no matter whether in dog or in man, has three factors which determine the outcome of the

process, namely, dosage, virulence and resistance. These factors may be influenced individually or collectively. The introduction of an anesthetic and an operation reduce the resistance both locally and generally and enhance the virulence. The dosage is important. However, with surgical intervention the damage done to the resistance of the patient is greater than the beneficial results obtained by decreasing the dosage. Therefore, we feel that the patient has a better prognosis if there is no operation. This we have demonstrated experimentally and clinically, and it is in accord with fundamental principles of bacteriology.

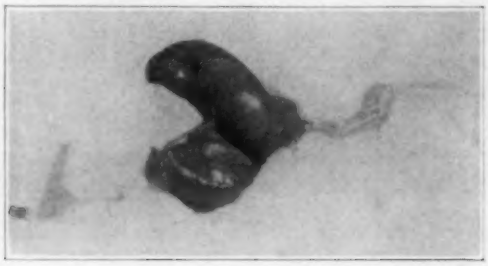

Fig. 5.—An appendix with one small omental adhesion to its base.

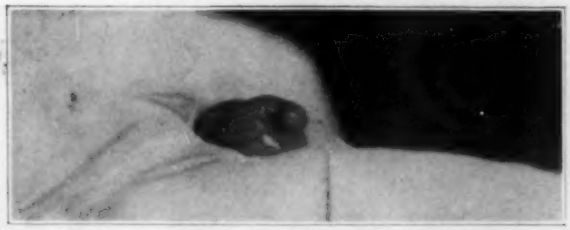

Fig. 6.—A typical coiled appendix without adhesions three months after appendicitis had been produced experimentally.

CONCLUSIONS

We believe that the following definite deductions can be drawn:

1. The cause of death in the majority of cases of acute appendicitis is generalized peritonitis, and conservative treatment causes a lower mortality than operative treatment (29 per cent conservative; 52 per cent operative).

2. Adhesions in the peritoneal cavity are distinctly increased by operative procedure and drainage (more than doubled in our experiment).

EXPERIMENTAL BURNS

I. THE RATE OF FLUID SHIFT AND ITS RELATION TO THE ONSET OF SHOCK IN SEVERE BURNS

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CHICAGO

There is still much diversity of opinion as to the mechanism of production of the clinical picture in the early stages of heat burns. Wilson [1] divided the effects of severe burns into four stages: (1) primary shock, (2) secondary shock, (3) septic toxemia and (4) healing. There is considerable difference in the way various authors define primary shock; some separate it from secondary shock by the time factor and others by the difference in the causative mechanism.

Using a time definition, Blalock [2] stated:

> Primary shock, or collapse, refers to the condition in which a decline in the blood pressure and the appearance of the symptoms of shock are noted immediately following the injury. In secondary shock, the time interval separating the injury and the appearance of symptoms is usually an hour or more. In some instances primary shock may progress into the secondary type.

Wilson stated:

> Initial shock is of nervous origin, is similar in nature to fainting or syncope, but longer in duration, and is due to a primary disturbance of the vasomotor mechanism. . . . It arises immediately after the injury and in the majority of cases is transient and slight in degree, and is rarely of serious significance.

Using this interpretation of primary shock, Wilson found that only 2.5 per cent of eighty fatalities from burns occurred at this stage. It is to be realized that primary shock may be present in many cases and yet not be the cause of death. Robertson and Boyd [3] used a much looser definition of primary shock, including changes found up to twenty-four hours after burning. They stated: "Death from burning occurring within the first twenty-four hours is practically always due to primary shock." This accounts for the high percentage of deaths in the first stage in their cases, namely, 41 per cent of thirty-two deaths.

From the Douglas Smith Foundation, and the service of Dr. Edmund Andrews, Department of Surgery, University of Chicago.

1. Wilson, W. C.: Treatment of Burns and Scalds by Tannic Acid, Brit. M. J. **2**:91 (July 21) 1928.

2. Blalock, Alfred: Acute Circulatory Failure as Exemplified by Shock and Hemorrhage, Surg., Gynec. & Obst. **58**:551 (March) 1934.

3. Robertson, Bruce, and Boyd, Gladys: Toxemia of Severe Superficial Burns in Children, Am. J. Dis. Child. **25**:163 (Feb.) 1923.

From the experimental standpoint it is possible that not all the features of primary shock may be shown in a completely anesthetized animal. Psychogenic factors are obviously nonexistent, and neurogenic influences are not completely comparable to those in conscious human beings. However, Blalock [4] was able to produce a picture simulating neurogenic primary shock by striking the abdomens of anesthetized dogs with a flat board. It is possible that the effects produced in cases of burns are due to widespread damage to numerous nerve endings in the skin (Wilson) giving rise to vasodilatation reflexly through centers in the medulla. There is, however, no good experimental evidence that such a condition as primary shock exists in the case of burns. Johnson and Blalock [5] found that the blood pressure of dogs rose in some cases, although it usually fell during the process of burning. In three experiments reported later in the present article the blood pressure taken during burning was as follows: In experiment 5 it rose from 114 to 146 mm. of mercury; in experiment 6 it rose from 120 to 160 mm., and in experiment 8 it fell from 132 to 116 mm. Underhill and Kapsinow [6] stated that primary shock never exists in anesthetized animals unless some part of the central nervous system has been subjected to the heat.

The third stage of the effects of severe burns is more a problem of secondary infection and not a direct result of the burn itself. Only 2.5 per cent of the eighty fatalities in Wilson's cases of burns occurred in this stage. Patients in the fourth or healing stage come under the province of the plastic surgeon. It is chiefly with the second stage of burns, the period of secondary shock, that the present paper has to deal. Eighty per cent of the deaths in Wilson's cases occurred in this stage.

SECONDARY SHOCK FOLLOWING BURNS

Secondary shock following burns is similar to secondary traumatic shock following other types of injury. It was not until the general problem of traumatic shock was elucidated that a clear conception of the pathologic physiology of burns was obtained. A quotation from Phemister's [7] article in 1928 is the first recorded statement based on

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4. Blalock, Alfred: Effects of Primary Shock on Cardiac Output and Blood Pressure, Proc. Soc. Exper. Biol. & Med. **31**:36, 1933.

5. Johnson, G. S., and Blalock, Alfred: Experimental Shock: XII. A Study of the Effects of Hemorrhage, of Trauma to Muscles, of Trauma to the Intestines, of Burns and of Histamine on the Cardiac Output and on Blood Pressure of Dogs, Arch. Surg. **23**:855 (Nov.) 1931.

6. Underhill, Frank P., and Kapsinow, Robert: The Alleged Toxin of Burned Skin, J. Lab. & Clin. Med. **16**:823 (May) 1931.

7. Phemister, D. B.: The Vascular Properties of Traumatized and Laked Bloods and of Blood from Traumatized Limbs, Ann. Surg. **87**:806 (June) 1928.

experiment of the importance of local loss of fluid into the tissues in the production of secondary traumatic shock:

> Furthermore, necropsy examination of the traumatized limb showed increase in limb volume from hemorrhage which was sufficient to account for the fall in blood pressure. In fact, the volume of blood that it was necessary to withdraw intermittently in the course of an hour in order to kill an animal was always less than the increase in volume of the traumatized limb of the other animal, which was due very largely to hemorrhage in the tissues.

Two years later Blalock [8] and Parsons and Phemister [9] worked out the extent of this loss. These authors repeated the old experiments of Bayliss and Cannon [10] but amputated the traumatized limb at a higher level. They compared the weight of the traumatized and of the opposite normal limb. Parsons and Phemister found this difference sometimes to be as much as 60 per cent of the total volume of blood. Later Blalock [11] used this bisection method to determine the local loss of fluid in cases of burns, and he found that as in cases of traumatic shock the local loss of fluid was sufficient to account for the death of the experimental animals.

Underhill, Kapsinow and Fisk [12] approached the problem of burns directly and came to practically the same conclusions as Blalock. From the work of these authors a brief résumé of the changes in secondary shock from a burn may be made as follows: Following a severe burn there is a gradual leakage of fluid from the blood stream into the burned tissues. This fluid has about the same concentration as blood plasma, its chloride content being a little higher than that of plasma and its sugar and nonprotein nitrogen contents about the same and its protein content being at least 80 per cent of that of plasma (Beard and Blalock; [13] Underhill,

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8. Blalock, Alfred: Experimental Shock: The Cause of the Low Blood Pressure Produced by Muscle Injury, Arch. Surg. **20**:959 (June) 1930.

9. Parsons, Eloise, and Phemister, D. B.: Haemorrhage and "Shock" in Traumatized Limbs, Surg., Gynec. & Obst. **51**:196 (Aug.) 1930.

10. Bayliss and Cannon, cited by Parsons and Phemister.[9]

11. Blalock, Alfred: Experimental Shock: VIII. The Importance of the Local Loss of Fluid in the Production of the Low Blood Pressure After Burns, Arch. Surg. **22**:610 (April) 1931.

12. Underhill, Frank P.; Kapsinow, Robert, and Fisk, Merl E.: Studies on the Mechanism of Water Exchange in the Animal Organism: I. The Nature and Effects of Superficial Burns, Am. J. Physiol. **95**:302 (Nov.) 1930; II. Changes in Capillary Permeability Induced by a Superficial Burn, ibid., p. 315; III. The Extent of Edema Fluid Formation Induced by a Superficial Burn, ibid., p 325; IV. The Composition of Edema Fluid Resulting from a Superficial Burn, ibid., p. 330; V. The Relationship of the Blood Chlorides to the Chlorides of Edema Fluid Produced by a Superficial Burn, ibid., p. 334.

13. Beard, J. W., and Blalock, Alfred: Experimental Shock: VIII. The Composition of the Fluid that Escapes from the Blood Stream After Mild Trauma to an Extremity, After Trauma to the Intestines and After Burns, Arch. Surg. **22**:617 (April) 1931.

Kapsinow and Fisk [12]). The amount of this fluid was determined by cutting out the edematous tissues and weighing them after evaporation at constant temperature (Underhill, Kapsinow and Fisk [12]) and by bisection of the animal and comparison of the weight of the burned with that of the normal half (Blalock [11]). The former authors found that definite fluid had collected in six hours and continued to accumulate up to from twenty-four to thirty-six hours. In twenty dogs after an average of twenty-seven hours this fluid averaged 1.4 per cent of the body weight. The latter author found the average fluid after an average of fifteen hours equal to 3.34 per cent of the body weight in eighteen dogs. The difference in the amounts of fluid observed by these two authors is to be explained partly by the difference in method and partly by the difference in the severity of the burn. The burns in Underhill's animals were not severe enough to produce death, while nine of Blalock's eighteen dogs died following the burning. In animals such as the dog there is no blistering or weeping from the skin, but in human beings there is this additional factor affecting the loss of fluid. One of the actions of tannic acid as used in man by Davidson [14] and Wilson [15] is to stop this additional loss of fluid.

Because of this local loss of fluid there is a decrease in the volume of blood as shown by Roome, Keith and Phemister [16] for traumatic shock in general and by Blalock for burns in particular. This reduction in the volume of blood is accompanied by a reduction in cardiac output.[5] Vasoconstriction accompanies this reduction in cardiac output, and it is not until this falls as low as one third its normal value that the blood pressure falls appreciably. When this stage is reached the fall in blood pressure may be quite rapid. Along with these changes in the circulation are changes in the composition of the blood itself. In Underhill, Carrington, Kapsinow and Pack's [17] series of twenty-one patients who were burned in a theater fire at New Haven, the hemoglobin varied from 117 to 209 per cent. The extent of this rise in hemoglobin is of interest because in the experiments reported in the present paper I did not find such a marked rise at any time in animals dying of experimental burns. In Blalock's experiments the rise in hemoglobin was not so marked as in Underhill's patients, and in animals severely burned by

14. Davidson, E. C.: Tannic Acid in the Treatment of Burns, Surg., Gynec. & Obst. **41**:202 (Aug.) 1925.

15. Wilson, W. C.: The Modern Treatment of Burns and Scalds, Practitioner **129**:183 (July) 1932.

16. Roome, N. W.; Keith, W. S., and Phemister, D. B.: Experimental Shock: The Effect of Bleeding After Reduction of the Blood Pressure by Various Methods, Surg., Gynec. & Obst. **56**:161 (Feb.) 1933.

17. Underhill, Frank P.; Carrington, George L.; Kapsinow, Robert, and Pack, George T.: Blood Concentration Changes in Extensive Superficial Burns, and Their Significance for Systemic Treatment, Arch. Int. Med. **32**:31 (July) 1923.

Underhill, Kapsinow and Fisk the rise in hemoglobin was also not so marked. These authors showed that the blood concentration often diminished just before death.

The point of view expressed in the preceding paragraphs has not been universally accepted as the entire explanation of the secondary shock stage of burns. This stage is often called that of toxic shock, the very name indicating a theory as to its causation. Bardeen,[18] in 1898, performed necropsies on five patients who died following severe burns. He found extensive changes in the lymphatic tissues, especially focal necroses of the germinal centers of the lymph glands and of the malpighian corpuscles of the spleen. He interpreted these changes as evidence of toxic action. Fender[19] studied the lymphatic tissues of burned rabbits, and although he found the same changes as Bardeen he came to less definite conclusions as to their origin, stating: "The theory of causation of death by a toxin cannot be said to rest upon adequate experimental work at present." Duodenal ulcer following burns has often been reported in the literature, the first descriptions being by Long[20] in 1840 and Curling[21] in 1842, and this has often been cited as evidence for the toxic theory. Underhill, Kapsinow and Fisk have shown, however, that in cases of burns produced experimentally on the trunk the intra-abdominal temperature may reach a very high point. It is quite possible that the changes found by Bardeen,[18] Fender,[19] Long[20] and others may merely be due to the physical effects of local hyperthermia. Blalock[22] has shown that generalized degenerative changes in some of the organs in dogs may result from hemorrhage alone. The same might be expected from the local accumulation of fluid in cases of burns without the interaction of any toxic agent. Only one necropsy has been performed at the University of Chicago Clinics in a case of fatal burn. This was performed on a 4 year old girl who died eleven days after a severe burn from hot water involving chiefly the anterior portion of the trunk. A typical Curling ulcer was found on the posterior wall of the duodenum 5 cm. below the pylorus. This ulcer might well have been on an infectious basis since three days before death there developed arterial and venous thrombi in the right arm and a large peritonsillar abscess from which Streptococcus viridans and Staphylococcus aureus

18. Bardeen, C. R.: A Review of the Pathology of Superficial Burns, with a Contribution to Our Knowledge of the Pathological Changes in the Organs in Cases of Rapidly Fatal Burns, Johns Hopkins Hosp. Rep. **7**:137, 1898.

19. Fender, Frederick A.: Lymphatic Pathology in Relation to the "Toxin" of Burns, Surg., Gynec. & Obst. **67**:612 (Nov.) 1933.

20. Long, cited by Bardeen.[18]

21. Curling, cited by Bardeen.[18]

22. Blalock, A.: Traumatic Shock and Hemorrhage, South. M. J. **27**:126 (Feb.) 1934.

were cultured. This case is also not inconsistent with Underhill, Kapsinow and Fisk's theory that the physical effects of the local heat are the important factor, since this patient's burns were chiefly over the anterior surface of the trunk.

The chief advocates of the toxic theory in recent years have been Robertson and Boyd,[23] who stated that "from a purely clinical point of view there seems to be no doubt that the burned tissues are responsible for the production of some toxin which is taken up by the blood stream." They went so far as to say that their toxin had a thermostable neurotoxic and a thermolabile necrotoxic element and contained primary and secondary proteoses. They found that blood or red cells from a burned animal when injected into normal animals produced all the symptoms of burn toxemia but that plasma alone produced no effects. From this they concluded that the toxin is present in or is adsorbed on the red cells. Alcoholic extracts of burned skin when injected into normal animals produced all the symptoms of burn toxemia, while skin from normal animals or from animals burned after death produced no such symptoms. Other authors have obtained results completely at variance with those of Robertson and Boyd. Underhill and Kapsinow's results indicate that the alcohol used in preparing Robertson and Boyd's extracts was the toxic agent and furthermore that normal skin was as toxic as burned skin. Underhill and Kapsinow found no difference following the injection of blood from burned animals and normal animals. They pointed out that Robertson and Boyd did not list their controls in detail, and finally stated: "Our experience with burns leads us to doubt the existence of a 'burn toxin,' and to believe that the persistence of this viewpoint is an obstruction in the way of clarification of the burn problem."

Other authors also obtained results which do not favor the toxic theory. Harkins, Wilson and Stewart,[24] working in Wilkie's laboratory, made extracts of normal and burned skin taken from rabbits at various intervals of from three minutes to forty-eight hours after burning. These extracts were prepared by the method of Chang and Gaddum [25] and were tested for acetylcholine equivalent as shown by the effect on the blood pressure of the cat and rabbit and on the rectus muscle of the frog. The active principle was found to be neither histamine nor acetylcholine, as the extracts were just as active in the rabbit given injections of atropine as in the rabbit or cat that did not receive the injections.

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23. Robertson, Bruce, and Boyd, Gladys L.: The Toxemia of Severe Superficial Burns, J. Lab. & Clin. Med. **9**:1 (Oct.) 1923.

24. Harkins H. N.; Wilson, W. C., and Stewart, C. P.: Depressor Action of Extracts of Burned Skin, Proc. Soc. Exper. Biol. & Med. **32**:913, 1935.

25. Chang, H. C., and Gaddum, J. H.: Choline Esters in Tissue Extracts, J. Physiol. **79**:255 (Oct. 6) 1933.

This indicates that the substance which was present in the approximate concentration of 1 microgram acetylcholine equivalent per gram of tissue was possibly similar to Euler and Gaddum's "P-substance." [26] Most important from the standpoint of the pathologic changes in cases of burns was the fact that the extract was equally potent when obtained from equal amounts of normal and of burned skin. Harris,[27] working in Lewis' laboratory and using earlier methods, found that up to thirty minutes the "histamine-equivalent" of burned and of unburned skin was the same, but one hour after burning the potency of burned skin was only 50 per cent that of normal skin. The later work of Harkins, Wilson and Stewart indicates that there is no detectable histamine in normal or in burned skin.

Harrison and Blalock [28] also found no evidence of burn toxin in their experiments. They found that transplantation of burned skin had no effect on the recipient, that débridement of the burned area markedly shortened the survival period of dogs and that transfusion of blood from burned to normal dogs was practically without effect. Underhill, Kapsinow and Fisk found that absorption of phenolsulphonphthalein and strychnine was very slight from burned areas. The work of Parsons and Phemister,[9] who tested the toxic properties of blood from traumatized limbs, has an indirect application to the problem of burns. These authors found that blood from a traumatized limb circulated through the femoral artery of another dog by Anrep's viviperfusion apparatus produced no vasodilation unless the blood itself was traumatized outside the body, and then it acted no differently from similarly treated normal blood. The effect of extracorporeal trauma was thought to be due to hemolysis. Parsons and Phemister also showed that in traumatic shock hemolysis could not be a factor because blood taken from the jugular vein of dogs suffering from the effects of severe trauma to the extremities showed no hemoglobin in the plasma.

At the present time, therefore, the two chief theories as to the causation of secondary shock in cases of burns are the toxic theory which postulates that the shock is due to a burn toxin and the physical theory which states that the shock is due to local loss of fluid from the blood into the burned tissues. The physical theory involves: (1) a local leakage of fluid into the burned tissues; (2) a resultant change in circulation including diminished volume of blood, diminished cardiac output and finally collapse of blood pressure, and (3) a resultant concentration of

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26. Euler, U. S., and Gaddum, J. H.: An Unidentified Depressor Substance in Certain Tissue Extracts, J. Physiol. **72**:74 (June 6) 1931.

27. Harris, Kenneth E.: Observations upon a Histamine-Like Substance in Skin Extracts, Heart **14**:161 (Dec.) 1927.

28. Harrison, W. G., Jr., and Blalock, Alfred: A Study of the Cause of Death Following Burns, Ann. Surg. **96**:36 (July) 1932.

the blood with increased percentage of hemoglobin. To test the time relation between certain of these changes by a continuous record the following experiments were devised.

METHOD

Animals under complete anesthesia were used in all experiments, and none that were burned were allowed to recover. Except for one rabbit, dogs were used in all experiments. They were weighed accurately and anesthetized with sodium barbital (0.3 Gm. per kilogram of body weight intraperitoneally), occasionally supplemented by a little ether. The blood pressure was determined by placing in the carotid artery a cannula which was connected to a mercury manometer. The percentage of hemoglobin was determined by the Sahli method, and hematocrit readings were made with the Van Allen hematocrit. The hair was removed from the body and extremities of the animals by the use of either fine clippers or a razor. The longitudinal midlines on both the dorsal and the ventral surface were marked with india ink. Female animals were catheterized so as to prevent urination during the experiment and consequent loss of fluid. If the animal had a long tail it was fastened to the midline of the abdomen so as to prevent movement during the experiment. The animal was then encased in a plaster cast covering all parts except the extremities and the tip of the snout. The openings in the cast were symmetrically enlarged so as to expose the chest and axilla on each side, and an opening was made over the front of the neck for insertion of the tracheal and carotid cannulas. The animal was then placed on the tipping apparatus devised by me.[29] An animal placed on this apparatus is in a state of balance, and any lateral shift in fluid will cause it to tip with a resultant change in the position of the marker on the kymographic drum. In earlier experiments[29] the openings in the cast were made only on the side to be burned. This had the disadvantage of causing a tipping of the apparatus at each breath, because the exposed side of the chest would puff out and cause an increase in weight. Furthermore, in certain control experiments as the animal relaxed when near death it would sag toward the exposed side. In all later experiments, therefore, the openings were made symmetrically.

Strips of wet plaster were placed along each side of the animal between the body cast and the balanced tray. This, when hardened, produced a solid union between the animal and the tray. An additional feature was the application of cuffs similar to those on operating tables to hold the front paws rigid but at the same time not stretched too tightly above the head. This was done for two reasons: First, when the paws were fastened too tightly with ropes they tended to become edematous, and it was thought that this edema if not symmetrical might cause tipping, and second, in certain early tracings the blood pressure showed the type of antemortem rise seen in cases of asphyxia such as might be produced by interfering with the accessory movements of respiration.

Control balance and blood pressure tracings were started, and blood was obtained by puncture of a hindpaw for an estimation of the percentage of hemoglobin and the hematocrit reading. The exposed limbs, inguinal region, chest and axilla on one side were then burned over a period of ten minutes by the direct application of a bunsen flame, chiefly from below through the holes in the tray. The resultant fluid shift to the burned side was recorded as a tracing. The tracing

29. Harkins, Henry N.: Shift of Body Fluids in Severe Burns, Proc. Soc. Exper. Biol. & Med. **31**:994 (May) 1934.

was continued until death, the blood pressure being taken intermittently and the percentage of hemoglobin and the hematocrit readings being determined at approximately hourly intervals. The sensitivity of the balance was then determined by counterbalancing the fluid shift by weights. It was observed at autopsy that in the sized animals used most of the edematous tissue was about 8 cm. from the midline of the tray. Hence the counterbalance weights were placed at this distance from the midline of the tray and at the same distance above the tray as the regions that tended to be most edematous. This was called the counterbalance method of determining the fluid shift. It is obviously quite rough but is probably as accurate as the second method used. The entire animal was then removed from the cast and weighed to determine the total loss of weight. It was bisected up to the neck by the method of Blalock,[11] and the two lateral halves were weighed after the head, tail, viscera, diaphragm and spinal column were discarded. This was called the direct weight method of determining the fluid shift.

The chief inaccuracy of the counterbalance method is the choice of the distance from the midline to apply the weights. The extreme limits of error in one experiment were determined as follows: At 8 cm. the counterbalance method gave a

TABLE 1.—*Variation in a Series of Seven Control Dogs, Blalock's Bisection Method Being Used*

Experiment	Weight of Dog, Gm.	Weight of Right Side, Gm.	Weight of Left Side, Gm.	Difference, Gm.	Difference as per Cent of Body Weight
9	4,600	1,237	1,265	28	0.61
10	5,862	1,492	1,537	45	0.77
11	6,090	1,643	1,603	40	0.66
18	24,000	6,948	6,920	28	0.12
20	11,460	3,643	3,620	23	0.20
21	24,000	6,948	6,920	28	0.12
23	12,070	3,643	3,620	23	0.19

fluid shift of 130 Gm. The burned region extended from 3 cm. from the midline to 13 cm. from the midline of the tray. If 3 cm. was used, the counterbalance method gave a fluid shift of 380 Gm., and if 13 cm. was used it gave a fluid shift of 80 Gm. The error is considerably less than these limits, however. It is also obvious that since the balanced tray is suspended from above, the midline of the tray is not the same as the fulcrum of the balance. The sensitivity of the balance must be tested in each experiment since it varies with the weight of the animal according to the well known formula:

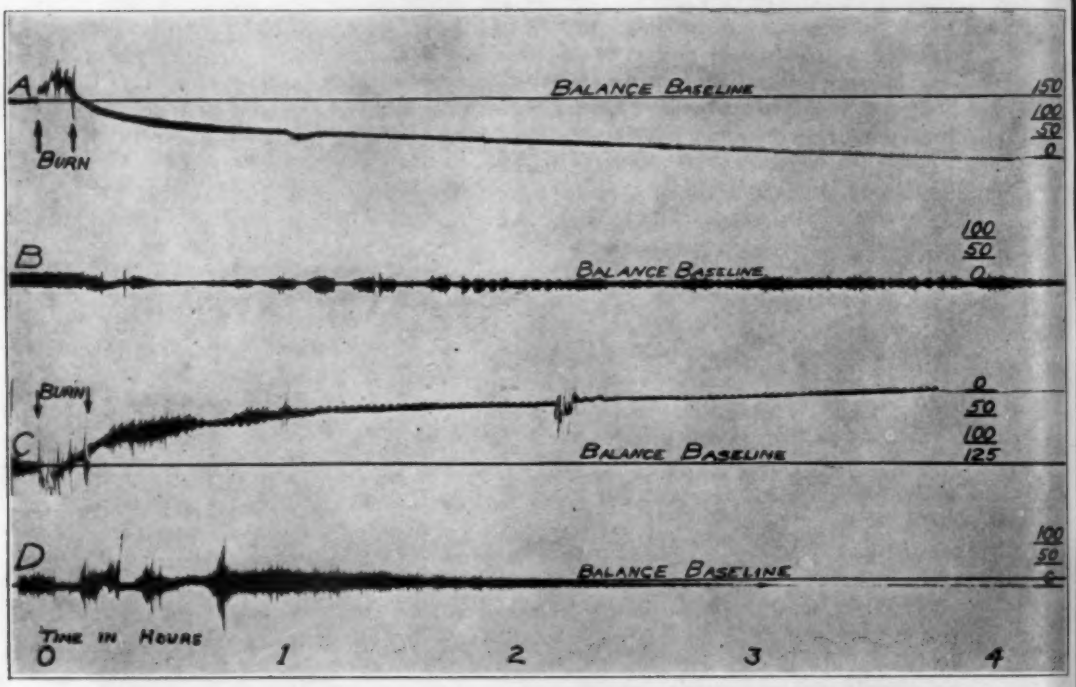
$$\text{Sensitivity} = \frac{\text{length of arm}}{\text{total weight system} \times \text{distance from center of gravity to fulcrum}}$$

The direct weight method is also not entirely accurate for small animals. Normal animals were bisected to test the accuracy of the method, the differences being shown in table 1.

RESULTS

Eight burn experiments and sixteen control experiments of various types were performed. In the eight burn experiments the interval between the application of heat and the death of the animal varied from one hour and thirty minutes to six hours and thirty minutes. In certain experiments there was a slight decrease in the weight of the burned side during the burning process as shown by a tipping of the apparatus to the opposite side. However, in most instances the burned side was

already heavier before the burning was completed. The fluid shift was rather rapid for some time and then became less rapid in the form of a decelerating curve till the time of death. The tracings show the results obtained in two typical burn experiments and two typical control experiments. The degree of shift in other experiments is given in table 2, from which it is seen that at the end of an hour from 41 to 77 per cent of the ultimate shift had already occurred. This suggests that even one hour may be too long an interval in which to include primary neurogenic shock if the time definition of primary shock is used. On



Tracings obtained in two burn experiments and in two control experiments performed on the balanced apparatus: *A*, burn experiment 7; *B*, control experiment 11; *C*, burn experiment 6, and *D*, control experiment 9. In experiment 7 the burned side is away from the kymographic drum, so that the shift to the burned side causes the recording point to move downward. In experiment 6 the burned side is toward the drum, and the shift causes the recording point to move upward.

the other hand, it might be objected that the fluid shift in certain instances was smaller in proportion to the body weight of the animal than the results obtained by other authors; e. g., in eight experiments the shift at death averaged 2.2 per cent of the body weight, whereas in nine experiments of Blalock it averaged 3.2 per cent of the body weight at death. Thus the restraining effect of the cast on respiration may have caused the animals to die sooner than otherwise.

To determine the amount of weight lost during the process of burning alone, animals were weighed before and after burning. A live animal lost 12 Gm. during burning of the right side for ten minutes. After burning of the left side for five minutes it lost an additional 10 Gm. A dead dog lost 10 Gm. in five minutes and 17 Gm. in ten minutes of burning of the right side. In each case an equivalent area was burned. It thus seems that the actual burning alone causes little loss of weight. By weighing the animal just before and at the end

TABLE 2.—*Fluid Shift in Eight Burn Experiments Performed on the Balanced Apparatus* *

Experiment	1	2	3	4	5	6	7	8
Weight, Kg.	3.3	5.0	4.0	5.0	5.9	5.2	6.3	6.5
Fluid shift in:								
10 minutes	..	0	0	24	35	13	0	−21
20 minutes	..	25	17	..	54	33	19	14
30 minutes	..	32	25	56	62	50	31	32
45 minutes	..	46	33	60	69	57	38	39
1 hour	..	41	42	64	77	67	46	46
1 hour 30 minutes	..	51	67	70	100	73	58	57
2 hours	..	57	75	72	..	77	65	61
2 hours 30 minutes	..	65	91	79	..	90	77	75
3 hours	..	70	100	84	..	96	81	86
3 hours 30 minutes	..	76	..	86	..	100	92	93
4 hours	83	81	..	88	..	..	100	96
4 hours 30 minutes	..	84	..	92	..	..	..	100
5 hours	..	87	..	96	..	..	..	..
5 hours 30 minutes	100	94	..	100	..	..	..	..
6 hours	..	97	..	..	..	..	..	..
6 hours 30 minutes	..	100	..	..	..	..	..	..
Time of death	5 hr. 30 min.	6 hr. 30 min.	3 hr.	5 hr. 30 min.	1 hr. 30 min.	3 hr. 30 min.	4 hr. 30 min.	5 hr. 15 min.
Shift by counterbalance	24	170	45	140	145	125	155	125
Shift as per cent of body weight	0.7	3.4	1.1	2.8	2.5	2.4	2.5	1.9
Weight of burned side	..	..	1,100	1,381	1,630	1,367	1,822	1,890
Weight of normal side	..	..	1,011	1,251	1,543	1,206	1,687	1,755
Weight difference	..	..	89	130	87	161	135	135
Weight as per cent of body weight	..	..	2.2	2.6	1.5	3.1	2.1	2.1

* The fluid shift is calculated from the tracing and expressed as per cent of the final displacement. The negative shift at the end of ten minutes in experiment 8 denotes the temporary decrease in weight of the burned side.

of a complete experiment the total loss from burning, the fluid lost from the lungs and what little is lost from the skin of a dog were measured. An animal weighing 6.5 Kg. lost 55 Gm. in four hours; one weighing 7 Kg. lost 116 Gm. in four hours, and one weighing 6.5 Kg. lost 94 Gm. in ten hours. This represents an average loss in weight from all causes including burning of 2.5 Gm. per kilogram per hour. Roome and Wilson [30] observed five control dogs over an average period of forty-six hours and twelve minutes and anesthetized them with an average of 276 mg. of sodium barbital per kilogram of body weight. The loss of weight at the end of this period averaged 9.11 per cent of the body weight. This corresponds to 1.9 Gm. per kilogram per hour,

30. Roome, Norman W., and Wilson, Harwell: To be published.

which is only a little less than that lost per hour by the burned animals used in the experiments described in the present paper. Furthermore, Roome and Wilson's figures can be interpolated for a shorter period since they observed the loss of weight at different intervals of time and found that it was directly proportional to the elapsed time.

The blood pressure usually remained near the normal level until the animal was near death, at which time the pressure collapsed rather suddenly. The hemoglobin percentage and the hematocrit reading rose following the burn but fell slightly before death. This may be due to

TABLE 3.—*Comparison of Fluid Shift, Blood Pressure, Hemoglobin Percentage and Hematocrit Reading in Experiment 8* *

Time	Shift, per Cent	Blood Pressure	Hemoglobin, Percentage	Hematocrit Reading
Control	0	132	93	45
10 minutes	—21	140	..	..
20 minutes	14	144	..	..
30 minutes	32	142	..	..
45 minutes	39	...	..	..
1 hour	46	...	..	..
1 hour 30 minutes	55	124	109	59
2 hours	61	...	...	..
2 hours 30 minutes	75	130	138	58
3 hours	86	...	...	..
3 hours 30 minutes	93	112	130	60
4 hours	96	34	122	62
4 hours 15 minutes	100	0	113	56†

Anesthetic = 1.9 Gm. of sodium barbital
Animal weight = 6,500 Gm.
Animal weight at end = 6,445 Gm.
Loss of weight = 55 Gm., or 0.8 per cent of body weight
Weight of burned side = 1,890 Gm.
Weight of normal side = 1,755 Gm.
Weight difference = 135 Gm., or 2.1 per cent of body weight
Counterbalance difference = 125 Gm., or 1.9 per cent of body weight

* It is seen that the fluid shift is followed by an increase in blood concentration while the blood pressure remains almost normal until near death, when it suddenly collapses. The fluid shift is calculated from the tracing and expressed as per cent of the final displacement. The negative shift at the end of ten minutes denotes the temporary decrease in weight of the burned side.

† Last sample from heart's blood, immediately after death.

the lowered blood pressure diminishing the hydrostatic pressure within the blood vessels and allowing water to return from tissues. From this it seems that the fluid shift and changes in the concentration of the blood follow each other rather closely, while the blood pressure remains near normal, only to collapse at the end. This may indicate that in clinical cases the patient may be in a serious condition even though the blood pressure is near normal and that the shock is secondary shock. The changes are compared for a representative experiment in table 3.

Three successful control experiments were made identical with the burn experiments. They showed no fluid shift at the end of ten, twelve and seventeen hours. After this time the effect of the barbital wore off, and the resultant struggling caused a slight movement. The absence

TABLE 4.—*Changes in Blood Pressure, Hemoglobin Percentage and Hematocrit Reading in Six Control Dogs*

Experiment 10*				Experiment 11*				Experiment 21				Experiment 22				Experiment 23				Experiment 24			
Time of Observation, Hrs.	Blood Pressure	Hemoglobin Percentage	Hematocrit Reading	Time of Observation, Hrs.	Blood Pressure	Hemoglobin Percentage	Hematocrit Reading	Time of Observation, Hrs.	Blood Pressure	Hemoglobin Percentage	Hematocrit Reading	Time of Observation, Hrs.	Blood Pressure	Hemoglobin Percentage	Hematocrit Reading	Time of Observation, Hrs.	Blood Pressure	Hemoglobin Percentage	Hematocrit Reading	Time of Observation, Hrs.	Blood Pressure	Hemoglobin Percentage	Hematocrit Reading
Onset	130	80	29	Onset	132	106	53	Onset	154	86	40	Onset	134	109	54	Onset	136	112	48	Onset	118	85	43
5	122	80	31	0	132	112	50	10	142	88	42	10	138	113	52	9	130	113	49	9	124	84	41
15	118	88	37	14	140	105	51	15	128	78	40	14	132	103	49	14	120	112	47	19	116	91	42
19	114	75	41	..	...	...	..	24	128	67	33	18	136	103	49	16	102	91	41	..	...	..	..
Weight of dog				Weight of dog = 6 Kg.				Weight of dog = 24 Kg.				Weight of dog				Weight of dog				Weight of dog = 19.5 Kg.			
Before = 5.862 Kg.												Before = 12.975 Kg.				Before = 12.070 Kg.							
After = 5.558 Kg.												After = 12.711 Kg.				After = 11.922 Kg.							
Loss = 304 Gm.												Loss = 264 Gm.				Loss = 148 Gm.							
Weight of				Weight of				Weight of								Weight of							
Right side = 1.537 Kg.				Right side = 1.643 Kg.				Right side = 6.948 Kg.								Right side = 3.643 Kg.							
Left side = 1.492 Kg.				Left side = 1.603 Kg.				Left side = 6.920 Kg.								Left side = 3.620 Kg.							
Difference = 45 Gm.				Difference = 45 Gm.				Difference = 28 Gm.								Difference = 23 Gm.							

* Additional balance tracings performed in experiments 10 and 11 showed no shift.

of shift in two of these controls is shown in the tracing. A control was made by burning plaster of paris of about the same age as that used on the experimental animals on the balance and by burning a dead dog in a plaster cast. The plaster alone showed a shift equivalent to a loss of weight of 14 Gm. during the burning but no further shift at the end of an hour. The dead dog lost 60 Gm. during the burning (counterbalance) or 63 Gm. (direct weight), and shifted back toward normal an estimated amount of 20 Gm. in seventy-five minutes. All of these changes are less than the shift produced by burning live animals.

Six control experiments were made to determine the changes in blood pressure, hemoglobin percentage and hematocrit reading in unburned animals placed on the apparatus. They show (table 4) that the changes in blood pressure, percentage of hemoglobin and hematocrit reading are all less than those produced by burns.

COMMENT

The results of these experiments are in general agreement with those of workers who advanced the hypothesis that local loss of fluid from the blood vessels into the burned tissues is a factor in the production of shock and that the type is secondary. A graphic method of recording the accumulation of this fluid shows that the method of producing burns used in the experiments caused the accumulation to be quite rapid. In several experiments more than half of the ultimate amount of fluid had collected in an hour. The total amount of fluid shift was not as great as that reported by some other observers but this may be because of its rapid formation. The concentration of the blood as shown by increase in the percentage of hemoglobin and in the hematocrit reading was roughly proportionate to the loss of fluid, but the blood pressure remained near normal until death approached, and then it fell rapidly.

The time relations of the various local, circulatory and hematologic changes in cases of shock are of importance in the differentiation of its various types. Experimental shock may be classified as primary and secondary, the decrease in blood pressure being said to precede reduction in cardiac output in the former and to follow it in the latter. Little evidence for primary shock was found in the experiments reported in the present paper. The accumulation of fluid in the burned tissues begins in many cases before the burning is completed, and the rapidity of this accumulation may account for many of the cases that have been mislabeled primary neurogenic shock. Psychogenic factors have been excluded from these experiments, and neurogenic influences could not be demonstrated although they could not be excluded. The accumulation of fluid in the tissues has been shown to be of importance, and this places the reaction in the category of secondary shock.

SUMMARY

A graphic method of recording the local accumulation of fluid in cases of burns is presented. This accumulation begins at the time of the burn and continues in the form of a decelerating curve until death. Accompanying the collection of fluid is a simultaneous increase in the concentration of blood as shown by an increase in the percentage of hemoglobin and in the hematocrit readings. After most of the fluid has accumulated, the fall in blood pressure sets in and continues rapidly until death occurs in a state of secondary shock.

A STUDY OF DISRUPTIONS OF ABDOMINAL WOUNDS

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Within the past year, the subject of disruption of abdominal wounds has enjoyed a belated prominence in the writings and at the meetings of surgeons. Sporadic papers had been published in the leading journals, but on Nov. 8, 1933, an entire evening's symposium by five leading surgeons of New York [1] was presented by the New York Surgical Society. Therein it was revealed that the incidence of this postoperative disaster was as high as 2 per cent, with a mortality rate ranging from 28 to 53 per cent.

Several of the participants in the aforementioned symposium contended that the incidence was undoubtedly higher because of the failure to recognize or record many of the cases. Similarly, Dr. Allen O. Whipple, who took part in the discussion, pointed out the inadequacy of statistics obtained from the record room as compared to those based on an accurate study of a series of laparotomies. With this in mind I have made a careful study of 1,560 laparotomies performed in all the services at the New York Post-Graduate Hospital over a period of a year and a half, from January 1933 to July 1934. Inguinal and femoral herniotomies, which might technically be considered laparotomies, were excluded from this series.

The particular condition of disruption of abdominal wounds has been known by many names, but regardless of the descriptive term used, the result is the same—a postoperative dissolution in the continuity of all the layers of tissue involved in the operative repair of the wound in the anterior abdominal wall, in part or in its entirety. In this respect, too, the statistics relating to incidence err, for it has been noted that in the contributions of some writers only the wounds that gape or from which viscera protrude are so classified. Thus, if this report were to deal only with gaping disrupted wounds my series of 20 cases would be reduced to 13, and if only the cases of evisceration were presented the number would shrink to 3. In presenting this study I have included all cases in which a partial or an entire separation of the abdominal

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From the Surgical Service, New York Post-Graduate Medical School and Hospital, Columbia University.

1. Meleney, F. L., and Howes, E. L.: Disruption of Abdominal Wounds with Protrusion of Viscera, Ann. Surg. **99**:5 (Jan.) 1934; Colp, R.: Disruption of Abdominal Wounds, ibid., p. 14; Grace, R. V.: Disruption of Abdominal Wounds, ibid., p. 28; White, W. C.: Disruption of Abdominal Wounds, ibid., p. 34; Heyd, C. G.: Disruption of Abdominal Wounds, ibid., p. 39.

wound from the skin through the peritoneum occurred. It was thought that only in this way could a fair analysis be made, despite the apparent increase in frequency.

A further fallacy of statistics per se is demonstrable. Based on a study of 1,560 consecutive laparotomies, the incidence of disruption is 1.28 per cent. It so happened that 6 dehiscences occurred in the last sixteen days of the eighteen month period. If the study excluded these disruptions the incidence for 1,500 cases would be 0.93 per cent. Again, if one were to consider only the cases of actual evisceration, of which there were but 3, the frequency would be 0.19 per cent.

Historically, the condition of rupture of a wound has unquestionably been an ominous occurrence since the inception of abdominal surgery. Over a quarter of a century ago reports are found by Ries [2] and Madelung [3] on the subject. The first author reported his experiences with a small group of cases in this country, while the second presented a series of 157 cases in Germany. Since that time intermittent reports have emanated from various centers on the globe, culminating in the monumental work of Sokolov [4] of Leningrad, U. S. S. R., who reported over 700 cases collected from the records of European surgeons to whom he directed his questionnaire. A truer idea of the prevalence of the complication may be gained from the knowledge that this number represents the response of only 233 of 1,140 surgeons to whom Sokolov sent his queries.

RÔLE OF VARIOUS ETIOLOGIC FACTORS

My prime incentive in undertaking this study was principally directed toward the etiologic factors involved, with the purpose of preventing as many complications of this kind as possible. Before entering into such a discussion, however, my group of cases will be analyzed. The appended table contains the salient features of this analysis.

Age.—The condition usually occurs in persons in the fourth, fifth and sixth decades of life. If the number of appendectomies is excluded from the total number of laparotomies performed, one finds that the ages of most of the operative subjects in this series fell in the period of the three decades just mentioned. Disruptions have been reported to occur in infants, especially in those with hypertrophic pyloric stenosis.

Sex.—This factor seems to play a rôle in that the incidence among males exceeds that among females. The ratio in this series was slightly

2. Ries, E.: On Post-Operative Separation of Laparotomy Wounds, Am. J. Obst. & Gynec. **60**:569 (Oct.) 1909.

3. Madelung, O.: Arch. f. klin. Chir. **75**:347, 1905.

4. Sokolov, S.: Post-Operative Rupture of Abdominal Wounds with Protrusion of Viscera, Vestnik khir. **65-66**:219, 1931; abstr., Internat. Abstr. Surg. (Surg., Gynec. & Obst.) **55**:157 (Aug.) 1932.

below 6:1. Sokolov reported a ratio of 2:1, whereas reversed values have been reported from centers in which most of the operations are performed for gynecological conditions. An important factor to consider is the apparent ability of most women to tolerate operations better than men who have worked hard, owing to economic strife, and who may show the effect of prolonged use, and abuse, of alcohol or nicotine. A factor may be the abdominal type of breathing in men, as compared to

Analysis of Twenty Cases of Disruption of Abdominal Wounds

	No. of Cases
Age, Years	
20–29	1
30–39	1
40–49	5
50–59	8
60–69	5
Sex	
Men	17
Women	3
Primary Illness	
Carcinoma	8
Disease of the biliary tract	6
Chronic pelvic peritonitis	2
Peptic ulcer	3
Cirrhosis of liver	1
Preoperative Condition	
Emaciation	12
Obesity	3
Jaundice	2
Arteriosclerosis	3
Postoperative Course	
Undue restlessness	15
Distention	15
Vomiting	14
Gastric lavage	12
Autolavage	2
Hiccup	9
Pulmonary complications	16
Type of Incision	
Superior right rectus	13
Inferior left rectus	3
Paramedian hypogastric	3
Right rectus para-umbilical	1
Drainage	
Employed	9
Not employed	11
Tension Sutures	
Employed	15
Not employed	5
Condition of Postoperative Wound	
Clean	13
Exposed to digestive ferments	3
Infected	4
Date of Disruption, Postoperative Day	
4th	1
5th	3
6th	3
7th	3
8th	3
9th	2
10th	0
11th	4
12th	1
Treatment	
Packing and strapping	6
Secondary suture	14
Outcome	
Living	9
Dead	11

the thoracic type of respiration in most women, who also have a greater elasticity of the abdominal wall.

Primary Illness.—Colp [1] has referred to the primary disease as the most important factor underlying the disruption of a wound. I shall discuss this assertion later in the paper in dealing with the etiologic factors. In 2 of the 8 cases of carcinoma the tumor was localized in the sigmoid flexure, in 2 cases in the stomach and in 1 in the ascending colon, pancreas, fallopian tube and testis, respectively. There were 128 cases of malignant growth among the 1,560 laparotomies, making the incidence of disruption 6.25 per cent, as compared to the frequency of 1.28 per cent for all cases. In all the 6 cases of disease of the biliary tract, cholecystitis, cholelithiasis and varying degrees of pancreatitis

were shown. In 2 cases choledochostomy was performed with insertion of indwelling T-tubes in the common duct. The 6 remaining cases included 2 of gastric and 1 of duodenal ulcer, 2 of chronic pelvic peritonitis with associated adnexal disease and 1 of cirrhosis of the liver in which an exploratory operation was performed.

Preoperative Condition.—The condition of the patient before operation is a substantial factor in predisposition to disruption of a wound. In 12 cases of the present series marked emaciation was shown, 1 patient, a man, having lost 40 pounds (18.1 Kg.) in one and a half months. Conversely, 3 patients showed marked obesity. Both emaciation and obesity, as will be shown later, have a physiologic relationship to dehiscence. Jaundice was present in 2 cases, and generalized arteriosclerosis in 3.

Postoperative Course.—Practically all the patients whose wounds subsequently disrupted had a stormy postoperative course, as indicated in the table. Restlessness, more marked than is normally seen postoperatively, was present in three fourths of the cases. Distention was marked in a similar number. The frequency of vomiting with subsequent gastric lavages was also high, while hiccup proved troublesome in 9 instances. Pulmonary complications occurred in 16 of the 20 cases cited. In 5 of these cases, the patients had definite bronchopneumonia. In all, 46 of the 1,560 subjects had pulmonary complications. This number represents a general incidence of 2.9 per cent, as compared to the prevalence of these complications in 80 per cent of the group with disruptions. Other observers have recorded the same high frequency for such postoperative complications as coughing, hiccup, nausea and vomiting and distention.

Operative Technic.—The elements inherent in the patient favoring disruption having been presented, the question of operative technic may be considered. Incisions in the epigastric region, especially the approach to the gallbladder and stomach through a high right or left rectus incision, show, both in this series and in the cases reported by other investigators, the greatest frequency of dehiscence. In order to better evaluate the relationship of the location of the incision to disruption, I have analyzed the total number of abdominal incisions. Five hundred and forty-five incisions were located in the right lower quadrant, all of which were low right rectus wounds with the exception of 2 McBurney incisions. None of the 545 wounds disrupted. Of 390 incisions in the right upper quadrant and the epigastrium 13 disrupted, an incidence of 3.3 per cent. Three of 501 incisions in the hypogastric region disrupted—an incidence of 0.6 per cent. Dehiscence occurred in only 1 of 69 paraumbilical incisions, and this was a reentry through a freshly healed wound. Three of a total of 49 low left rectus wounds disrupted. This

relatively high frequency is easily explained in that 2 were colostomy wounds and 1 was a fecal fistula, all of which became grossly infected. No dehiscence occurred among the 6 subcostal incisions. A false impression of the frequency of disruption with regard to localization results from isolated reports. For example, Madelung reported a series of 124 disrupted wounds below the umbilicus and only 16 above it. However, most of his operative cases were gynecological—hence the discrepancy in the statement that the majority of disruptions occur in the upper part of the abdomen.

Except for minor individual variations, the usual closure of a laparotomy wound employed at the New York Post-Graduate Hospital is effected for the peritoneum with no. 1 or 2 plain catgut in a continuous suture. The muscle is reunited by some surgeons with the same material. Fascia is apposed with no. 1 or 2 chromic gut in a continuous suture, and the skin is closed with black silk. Tension sutures of dermal suture material, silkworm gut or braided silk, either of the circular or of the lateral button type, are used at the discretion of the operator. In cachectic persons Erdmann,[5] who attributes many disruptions to the too rapid absorption of catgut due to what he terms "tissue hunger," often uses chromic catgut throughout or heavy braided silk in through-and-through sutures. In the average case sutures of the skin are removed between the eighth and the tenth day, and the tension sutures between the tenth and twelfth day. Binders are not applied as a routine. Some surgeons insist on their use, while others order them only in selected cases. There is no question of the support and counterpressure afforded by the binder to the patient who is coughing or vomiting. However, some surgeons believe that the attendant fixation of the upper abdominal muscles and the limitation of costal excursions in the bedridden patient predispose to pulmonary atelectasis.

In two thirds of the cases of disruption tension sutures of the dermal suture material, silkworm or braided silk were used. All of these sutures included fascia and were of the circular type, except in 2 cases in which lateral buttons were used. It is interesting to note that in 1 of these cases the intra-abdominal disruptive forces (coughing and vomiting) were such as to cause a spontaneous rupture of two of the silkworm tension sutures. Binders had been used in two thirds of the cases prior to, and were employed in all following, the repair of the disrupted wound. Drainage in the form of cigaret tampons, rubber tissue or iodoform gauze was used in 9 cases, while 11 wounds were closed without drainage.

Postoperatively, 13 of the wounds were clinically clean. Three were exposed to drainage from the biliary tract, while 4 were grossly infected after intestinal surgical procedure. In treating the patients with the

5. Erdmann, J. F.: Personal communication.

latter type of incisions, the wounds were purposely separated superficially, but complete dissolution followed the infection. Suppuration in wounds was shown by Howes and Harvey [6] to cause rapid absorption of even chromicized catgut. The day of the disruption of the wound, not always accurately determined, is indicated in the table. It is likely that the real dehiscence of the peritoneum and fascia occurred earlier than is indicated. Undoubtedly, the seepage of digestive ferments from the gastro-intestinal tract is a factor in the delay of healing of the wound. In the present series almost as many wounds with drainage disrupted as those which were closed tightly. It should be remembered, too, that roughly only 1 wound in every 10 of the total number was drained.

The disruptions of wounds reported in this paper occurred in the practice of eleven surgeons in different services at the New York Post-Graduate Medical School and Hospital. Eight house surgeons acted as first assistants at the operations. The point has been made that the tendency to pull on suture ligatures, the rough handling of tissues, the strangulation of tissue by ligatures tied too tightly or, conversely, the slipping of ligatures from faulty knots are all contributory to disruption of the wound. The wide distribution of cases just shown tends to prove that such defects in technic were accidental rather than due to a repeated error in performance by one person.

Few of the commentators on disruption of wounds have placed much stress on the importance of anesthesia. Colp stated: "It is quite evident that this plays an insignificant and unimportant part." Anesthesia in all the cases of disruption in this series was effected by gas and oxygen followed by ether. In 2 cases it was started with a spinal anesthetic, but persistent abdominal straining due to incomplete anesthesia necessitated recourse to ether. Since this study was completed 1 more dehiscence occurred, the patient having been under spinal anesthesia. Some workers may aver that the preponderance of disruptions in cases of inhalation anesthesia is merely a coincidence in a small series. Yet the sole anesthetic used in 154 of the 1,560 abdominal sections was spinal, and in this group, representing 10 per cent of the cases, no disruption occurred. Dr. Thomas H. Russell, of the staff of the New York Post-Graduate Medical School and Hospital has used spinal anesthesia for laparotomies whenever possible. He informed me recently that he has had, roughly speaking, 1 disruption in every thousand cases in the last five years. Of particular interest is the fact that Dr. Russell uses plain catgut for the peritoneum and fascia and never chromicized gut, which he believes to

6. Howes, E. L., and Harvey, S. C.: Strength of Healing Wounds in Relation to Holding Strength of Catgut Suture, New England J. Med. **200**:1285 (June 20) 1929.

be irritating to the tissues. From my studies I must conclude that inhalation anesthesia, with the ever present possibility of bronchial irritation or of major pulmonary complication together with distention, which is usually singularly absent with spinal anesthesia, plays a significant part in producing a stormy postoperative course and subsequent disruption of the wound.

Diagnosis.—While obvious in most cases, the diagnosis is often rendered difficult because of the insidiousness of the condition, especially when the appearance of the cutaneous incision belies the condition in the depth of the wound. Characteristically, profuse serosanguineous discharge appeared in 16 of the 20 cases in this series. It should be remembered that in the 4 remaining cases there was gross infection with purulent drainage. As has been noted, all the patients had rather eventful postoperative courses. That the nausea, vomiting and distention might have been the effect, rather than the cause, of the disruption is probable in a few cases. I have been impressed with the unusual amount of pain which several of the patients complained of prior to, and the marked well-being after, the disruption. There was no appreciable rise in the temperature or pulse rate, and the abdominal discomfort often disappeared after the accident. One patient frankly stated that he "felt something snap" in the area of the wound preceding the saturation of the dressing with serosanguineous fluid. In 4 of the cases dehiscence occurred within a few hours of the usual removal of the cutaneous sutures. A nurse's note on each chart recorded an antecedent spell of coughing in 3 cases and straining at stool in the fourth. In 2 other cases the sutures of the skin were removed to confirm the diagnosis. Lahey [7] recommended the exploration of the wound with a probe under strict asepsis in suspicious cases in which primary union of the skin exists. The various types of disrupted wounds and their appearance have been well described by Heyd.[1] I shall therefore pass over this aspect to a consideration of the methods of treatment.

Treatment.—The methods of treatment of disrupted wounds fall into two broad groups—that of packing and strapping and that of secondary suturing. The former method has been chosen most frequently as the conservative one in cases in which the condition of the patient was such as to forbid further intervention. Packing and strapping should, of course, be the initial procedure after the discovery of dehiscence, regardless of whether or not the patient will later be transferred to the operating room for resuture of the wound. In this group packing, usually with iodoform gauze, and strapping with broad adhesive tape were used for 6 patients, 4 being critically ill and 2 having only partially disrupted wounds.

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7. Lahey, F. H.: The Management of Some Complications Following Abdominal Operations, J. A. M. A. **89**:1735 (Nov. 19) 1927.

Fourteen of the disrupted wounds were resutured, the particular technic varying with the operator. For the most part, through-and-through tension sutures of dermal material, silkworm gut or braided silk, taking in all the layers, were used. In 2 cases silver wire was used, the repair in 1 case being a modification of the method described by Shipley [8] of using the wires as tension sutures, with gradual shortening laterally until the edges of the wound are coapted. The anesthetic used in 7 cases was 2 per cent procaine hydrochloride locally, while a spinal anesthetic was administered in 5 cases and gas and oxygen in 2, in which, of course, no indication of evisceration was shown. Reduction in all cases was satisfactory, and in none of the cases of resuture did subsequent breakdown occur. Pool [9] advised the restoration of prolapsed intestines to the abdomen as quickly as possible. To minimize shock and mechanical difficulties in replacing distended intestinal loops, he suggested the insertion of a needle of small caliber through the wall of the intestine and the application of suction. There has been no occasion to use this method.

A study of the mortality figures reveals the fact that disruption of a wound is often a complication of what would have been a fatal outcome in any event. Eleven of the 20 patients died, a mortality rate of 55 per cent. Peritonitis occurred in 4 cases, but this developed prior to the disruption, although it must be admitted that the further complication only hastened the fatal outcome. Pneumonia, cardiorenal disease and carcinomatosis each claimed 2 victims, while cirrhosis of the liver was the cause of death of 1 patient. The mortality rate in the cases of resuture was 50 per cent, while in those in which the treatment was packing and strapping a mortality rate of 66 per cent was shown. In 4 of the latter group, however, the procedure was palliative because of the inevitable outcome. Other surgeons [1] have reported mortality rates ranging from 28 (Colp) and 33 per cent (Sokolov) to 53 per cent (White).

REPORT OF "EPIDEMIC" OF DISRUPTIONS

Of particular interest in this study was the occurrence of an "epidemic" of disruptions of wounds in the surgical service of the hospital during a period of two weeks in June 1934. The cases included 3 in the wards and 3 private cases, and the patients were in the hands of 6 operators. The accumulated data on these cases have already been presented, but because of the importance and gravity of the situation they merit closer scrutiny and consideration. Such a grouping, seemed more than mere coincidence.

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8. Shipley, A. M.: Broken-Down Abdominal Incisions: A Method of Closure, Ann. Surg. **82**:452 (Sept.) 1925.

9. Pool, E. H.: Post-Operative Treatment, New England J. Med. **201**:510 (Sept. 12) 1929.

All the patients were men; 5 had epigastric incisions and 1 a right pararectus incision which, incidentally, was a reopening of a freshly healed wound for the secondary resection of a carcinoma of the ascending colon, an ileocolostomy having previously been performed. With the exception of the last case, in which the wound became infected and broke down, coughing of a persistent and racking nature occurred. More than average postoperative restlessness, with nausea, vomiting and marked distention (in 3 cases), was present. The anesthetics used in all cases were gas and oxygen followed by ether. In 1 case a spinal anesthetic was given, which failed. In 2 cases the characteristic profuse serosanguineous drainage preceded the removal of the sutures on the sixth postoperative day, while in 2 cases a similar drainage followed the removal of the silk from the skin on the seventh and eleventh day, respectively. In 2 cases in which a fatal outcome was inevitable, the disruptions were treated by packing and strapping. The 4 remaining patients were removed to the operating room within an hour or two of the accident, and resuture was performed. All 4 patients of this group recovered and left the hospital with apparently well healed wounds.

In analyzing the cases in the aforementioned group for a causative factor, particular suspicion fell on the material used for sutures. Tension sutures were utilized in 4 of the 6 cases. In all 6 a particular standard brand of no. 1 plain catgut (for peritoneum) and of no. 1 chromic catgut (for fascia) was used. Two other brands of catgut were also used in the operating rooms by operators with individual preferences, but in these 6 cases it was known that a newly arrived assignment of the catgut in question was employed. It is also true that other laparotomy wounds had been sutured with the same material during the same two week period, but the postoperative course in these cases was relatively uneventful.

Unfortunately, before definite evidence seemed to point to the catgut, the remainder of the stock was removed from the shelf and returned. Hence investigations of the tensile strength or quality of the catgut could not be carried out. It is my belief that in this particular group of disruptions the catgut was defective and failed in its normal duty of holding the tissues during the period of active healing of the wound in the face of the disruptive forces of cough, nausea, vomiting, distention and hiccup. In several of the wounds strands of catgut varying from ½ to 3 inches (1.27 to 7.62 cm.) in length were found with frayed ends, as if torn, the rest of the strand being intact except for slight swelling. It is probable that this particular batch of catgut, although it passed the minimum factory requirements, was poor in quality and deficient in tensile strength, because the same brand had been used previously without mishap.

ANALYSIS OF TYPICAL LAPAROTOMY

In undertaking a study of the underlying etiologic factors one may diverge for a moment and consider a typical laparotomy. A simple incised wound is made through the abdominal wall, cleanly dividing the anatomic layers of skin, fascia, muscle and peritoneum. In this process a certain portion of tissue is unavoidably destroyed, together with blood vessels and nerve filaments. Ligatures are applied to bleeding points, and sutures are used in the closure of the wound. The technic varies with the operator, but the fundamental steps are unchanged. Howes, Sooy and Harvey [10] described the phenomena of exudation of blood or plasma and subsequent formation of fibrin along the latticework of which fibroblastic proliferation occurred after closure of the wound. The whole response is one of restoration of continuity. Damaged cells are restored or replaced, and new capillary buds appear. As a result of this fibroplasia an attendant increase in the strength and contraction of the wound occurs.

Howes [11] showed that during the first four or five days, the so-called latent period in healing just described, the strength of the wound is dependent on the holding power of the sutures and on the nature of the tissues. The thread strength of the suture, he demonstrated, was relatively unimportant and independent of the size of the suture. Whipple [12] cited the tensile strength of laparotomy wounds in cats in which the wounds sutured with catgut broke through the site of the incision even on the eighth day and thereafter the break took place through the surrounding tissues. With repair by silk, the suture line tore as late as the sixth day, the surrounding tissues tearing from the seventh day on. After the latent period in the healing of a wound the regenerative phase occurs, with fibroblastic proliferation which reaches a peak from the twelfth to the fourteenth postoperative day. It is this later phase which adds strength to the wound, taking the burden of cohesion of the tissues from the suture material.

Because the present study deals entirely with wounds repaired with catgut, silk being used only for closure of the skin, I shall confine myself to a consideration of the absorbable suture. Microscopic studies of plain catgut in vivo by Howes and Harvey [13] demonstrated the cellular reaction about the embedded suture. After the first day the strand of catgut becomes swollen and its fibers separate. Thereafter, a progressive

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10. Howes, E. L.; Sooy, J. W., and Harvey, S. C.: The Healing of Wounds as Determined by Their Tensile Strength, J. A. M. A. **92**:42 (Jan. 5) 1929.

11. Howes, E. L.: The Strength of Wounds Sutured with Catgut and Silk, Surg., Gynec. & Obst. **57**:309 (Sept.) 1933.

12. Whipple, A. O.: The Use of Silk in the Repair of Clean Wounds, Ann. Surg. **98**:662 (Oct.) 1933.

13. Howes, E. L., and Harvey, S. C.: Tissue Response to Catgut Absorption, Silk and Wound Healing, Internat. J. Med. & Surg. **43**:225 (April) 1930.

diminution in the cross-section of the strand occurs, with complete absorption from the fourth to the sixth day. With chromic catgut there is less swelling of the strand, and absorption is delayed. During the regenerative period, after the first five days, fibroblasts proliferate at the periphery of the suture and occasionally in its interstices.

What I have just described holds true for healing under ideal conditions. Hemorrhage, extensive necrosis of traumatized cells and infection all hasten absorption of the gut and prolong healing of the wound. The regenerative phase of fibroplasia is dependent on the antecedent exudative phase, and if this initial period is prolonged so too will be the stage of actual healing of the wound. As a result of their experiments, Howes and Harvey recommended the use of gut of small size, such as no. 0, twenty day chromic gut, because such a strand will last through the period of healing and be absorbed shortly after healing is complete and because, owing to the smallness of the size, minimal trauma will be incurred and a minimal amount of foreign protein in the form of collagen will be left in the tissues. In addition, the limitations of the tensile strength of the smaller-sized catgut will prevent the unnecessary strangulation of tissue beyond the point of apposition, an abuse which a strand of larger size might easily permit. These workers calculated the various holding strengths of catgut per se in tissues. The holding strength of a stitch in fascia, the only tissue of sufficient density to resist the cutting power of a suture, varies from 7 to 8½ pounds (3.2 to 3.9 Kg.). On the other hand, the holding strength of a strand of no. 0 catgut is 9 pounds (4.1 Kg.). Thus, before the strand of catgut will break, it will tear through the tissue.

STUDY OF INTRA-ABDOMINAL PRESSURE

With the aforementioned conception of healing in wounds and the fate of suture material in vivo, a consideration of the important, yet often overlooked, factor of intra-abdominal pressure is in order. The abdominal cavity really represents the interior of a muscular bag. Externally, there is the atmospheric pressure of 15 pounds per square inch, while within the peritoneal cavity three factors—gravity, variations in the omental and mesenteric deposits of fat and variations in the size of the viscera—play their rôles. In an illuminating chapter Livingston [14] reported the results of a study of variations in pressure within the abdomen. In contrast to the negativity of intrathoracic pressure, the general intra-abdominal pressure practically equals that of the atmosphere. Pressures within and without regulate the configuration of the abdominal wall.

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14. Livingston, E. M.: Pressure Variations Within the Abdomen: A Clinical Study of the Abdominal Cavity and Peritoneum, New York, Paul B. Hoeber, Inc., 1932.

Each abdominal viscus has an intraluminary pressure of its own. Hence, the need of an intravisceral and an intra-abdominal balance of pressures. The ingestion of a heavy meal eventuates in an altered abdominal pressure, with the need of loosening the constricting apparel. Livingston pointed out the existence of an entero-abdominal reflex, which in this case resulted in relaxation of the abdominal wall, compensating for the increased intraluminary pressure. The storage of fat intra-abdominally in the mesenteric ligaments and extraperitoneal spaces represents nature's "buffer" to strengthen natural supports. Atonicity of viscera is a consequence of marked depletion of such fatty stores.

Clinically, the starvation and cachexia produced by a malignant condition result in the scaphoid abdomen, and, secondarily, the loss of fat is accompanied by a compensating atonic dilatation of the hollow viscera which accounts for the digestive and asthenic symptoms following in the wake of wasting illnesses. In this condition the anterior abdominal wall is passively driven inward by a greater external pressure. On the other hand, an increase in intra-abdominal pressure is responsible for the protuberance seen in the presence of obesity, ascites and the distention of intestinal obstruction.

The abdominal musculature likewise exhibits tonicity, and with the synchronous contraction of the muscular sac which forms the wall of the abdominal cavity, as in coughing, defecation or parturition, a temporary increase in pressure is produced. These groups of muscles can act synergistically or antagonistically. Variations in abdominal pressure are also produced by the thoracic, and especially by the abdominal, type of respiration.

I have taken the liberty to dwell at length on the healing of wounds, on the use of catgut and on intra-abdominal pressure as a premise to my contention that all three factors are closely interwoven in the production of disruptions of abdominal wounds. As has been shown, it is a rare case which does not show a constant source in a persistent or explosive type of increased abdominal pressure. Coughing, hiccup and retching, coupled with distention, were almost universal in this series of cases. Add to this disruptive force a point of lowered resistance, as represented in the laparotomy wound, and the sum spells trouble if the suture material, the healing of the wound or the technic of closure is inadequate.

Coffey [15] showed that, contrary to popular belief, the strong aponeurotic layers enclosing or forming terminal attachments for the muscles of the anterior abdominal wall are but slightly elastic under an ordinarily acute strain. He pointed out that the equilibrium of normal

15. Coffey, R. C.: Intravisceral and Intra-Abdominal Pressure, J. A. M. A. **69**:683 (Sept. 1) 1917.

intra-abdominal pressure is established by the intermittent expulsion of the liquid and gaseous visceral contents. However, it must be remembered that postoperatively, especially after general anesthesia, this safety-valve effect is often temporarily upset. Likewise, the entero-abdominal reflex, the regulating mechanism previously cited, is involved. Consider, then, the postoperative status in a case of laparotomy in which there is a clinically stormy course. Owing to operative trauma, the abdominal wall is splinted. Within the abdominal cavity a distended stomach or dilated intestinal loops produce increased pressure. Add to this condition spasmodic, forceful muscular contractions resulting from coughing, vomiting or expulsive efforts, and the strain on a weak operative wound might easily be sufficient to cause dehiscence.

Definite proof exists that the intra-abdominal pressure can often rise to such a level as to transmit considerable force to the anterior abdominal wall. Sporadic cases of spontaneous rupture of the rectus abdominis muscle, subsequent to violent contractions and without external violence, have been reported. Hume,[16] in discussing the etiology of nontraumatic acquired hernias, cited the important rôle played by intra-abdominal pressure in the actual production of herniation. He stated that during violent muscular effort the intra-abdominal pressure may rise to 100 or 150 mm. of mercury, owing partly to diaphragmatic descent but chiefly to the contraction of the anterior and lateral abdominal muscles, especially the transversalis abdominis.

Recently, Murphy and Mengert[17] carried out a study of intra-abdominal pressures created by voluntary muscular effort and measured by a distended balloon in the vagina. While this investigation was carried out as a study of the etiology of prolapse and of the relations of pressure in labor, these workers observed that the manometric column of mercury was set into simple rhythmic vibrations, with the column reaching a much higher level on the first upswing during sudden, sharp abdominal contractions, than when the muscular contraction was slow. Other workers have measured intra-abdominal pressure by inserting a tube in the rectum or a balloon in the esophagus or stomach, by means of a bell jar with a rubber diaphragm placed on the abdomen or even with a cannula penetrating the abdominal wall into the peritoneal cavity.

Clinically, this increase in pressure, uncompensated for by normal physiologic reflexes, produces both subjective and objective signs and symptoms. There is present a visible and palpable abdominal protuberance, and the patient complains of an oppressive type of pain.

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16. Hume, J. B.: Diaphragmatic Hernia, Brit. J. Surg. **19**:527 (April) 1932.

17. Murphy, D. P., and Mengert, W. F.: Intra-Abdominal Pressures Created by Voluntary Muscular Effort, Surg., Gynec. & Obst. **57**:487 (Oct.) 1933.

The lowering of this pathologically increased pressure by such therapeutic measures as the passage of the Levine tube in cases of acute gastric dilatation, an enterostomy in cases of intestinal obstruction or the effective use of the extract of the posterior lobe of the hypophysis or of spinal anesthesia in cases of paralytic ileus is attended by almost immediate relief to the patient. I have observed that patients, immediately after the disruption of their abdominal wounds, have a feeling of well-being and relief from severe abdominal discomfort. The explanation seems to be that there is an immediate release of intra-abdominal pressure which was created by intravisceral distention. Persistent coughing, with its resultant strain on the abdominal wall, produces sudden increases in intra-abdominal pressure which may easily throw an unbearable strain on the fresh suture line.

CLINICAL TYPES SUSCEPTIBLE TO DISRUPTION

In the light of what has been said concerning abdominal pressures, the various types of subjects in whom abdominal wounds disrupt may be considered. The high percentage present in cases of chronic infection or of a malignant growth with attendant cachexia and anemia is attributed by some investigators to poor regenerative powers of the tissues to promote firm healing, while others attribute the dissolution of wounds to "tissue hunger" and the resultant hasty digestion of catgut. There is, in my opinion, one characteristic finding in cachectic patients, no matter what the cause, and that is depletion of the stores of fat, both in the abdomen and elsewhere. The viscera are in an atonic state, and the muscular abdominal sac has little, if any, fatty "buffer" layer which might normally absorb or diffuse a sudden or constant propulsive force arising intra-abdominally from cough, distention or vomiting. A similar situation holds in the cases of hypertrophic pyloric stenosis, a condition in which, according to some observers, disruption of wounds is relatively frequent.

Conversely, the markedly obese patient also presents a problem as far as disruption is concerned. Here, if my assumptions are correct, there is an undue increase in intra-abdominal pressure due to an abnormal deposition of fat, both in the abdominal wall and in the visceral mesenteries and omentum. These patients are poor subjects for anesthesia and are susceptible to respiratory complications. Closure of the abdomen at the termination of an operation is often technically difficult and attended with tearing of the sutures. No better example of such a situation and its remedy is seen than in the case of a large ventral hernia in an obese person, which would defy the surgical ability of a master. Yet, if such a patient is placed on a rigid dietary regimen resulting in appreciable loss of weight, the later repair, closure and postoperative course are uneventful.

From this line of reasoning it must be conceded that the sutured incised wound in the anterior abdominal wall is subjected in a stormy postoperative course to many sudden or constant stresses and strains. This is especially true of wounds in the epigastrium, in which separation of the costal arch with each respiration exerts a lateral pull on the attached muscles and the suture line. Furthermore, the rectus muscles widen and are thinned toward their costal insertions, providing a point of anatomic weakness. According to Howes and Harvey, the suture loses 50 per cent of its strength when the wound has obtained 50 per cent of its maximum strength. This holds true in a normal case. Excessive oozing or necrosis in the wound and a mild infection would admittedly delay healing and increase the rate of absorption of catgut. A slipped knot, the tearing of a frayed strand of catgut, the cutting through of the suture or the strangulation of the sutured tissue would all present points of lowered resistance, easily giving way under an undue strain.

Ries [2] reported 2 cases in which the snapping of the catgut, after it had been used to close a wound, was audible. These accidents, by fortuitous circumstances, were recognized and rectified. In 1 of the cases the patient stated that he "felt something snap." In several of the cases of disruption of abdominal wounds which I have personally observed, catgut in varying lengths was noted in the wounds. The frayed ends of several of the pieces suggested the possibility that the strand of catgut gave way under strain. This has already been alluded to in commenting on the incidence of 6 disruptions in a period of two weeks.

PROBLEM OF SUTURE MATERIAL

This brings one to a vital point in the use of suture material, especially of catgut. Despite efforts of the committee on Catgut Standards of the American Medical Association, no agreement has been reached among manufacturers on a standard test for catgut. As a result surgeons must depend on the statements of the various producers as to the quality of their products. Some firms judge the absorbability and tensile strength by experimentation with animals and others by tests in vitro with proteolytic enzymes; still others use the chromicizing process for regulation of the absorbability. Obviously, standardization is necessary.

Kraissl and Meleney [18] recently devised an apparatus for testing the tensile strength of strands of catgut against the digestive action of a standard solution of trypsin. They found a variation in the rates of digestion of various brands of catgut of both native and foreign

18. Kraissl, C. J., and Meleney, F. L.: A Method for Determining the Time of Catgut Digestion in Vitro, Surg., Gynec. & Obst. **59**:161 (Aug.) 1934.

manufacturers. These workers were of the opinion that the problem can be solved only by analysis of the catgut in vivo and in vitro—hence the presentation of their accurately controlled test tube method adapted to standardization. Misleading statements by manufacturers were cited in which a certain brand of catgut was said to hold tissues for ten, twenty or forty days, while another brand was described as being able to resist complete absorption for ten, twenty or forty days. I have already shown that the benefits of catgut are lost long before it is completely absorbed.

Specialized technics and usages of suture material have been developed by some operators with uniformly good results, as indicated by their reports. Colp, noting the tendency of median epigastric incisions to disrupt, frequently used through-and-through sutures of braided silk, which were removed on the fourteenth day. By this altered method disruption of this particular type of incision was practically eradicated. Kennedy,[19] drawing on the combined surgical experiences of himself and his predecessor, Dr. Joseph Price, during fifty-six years, reported that not a single disruption of an abdominal wound occurred with the use of through-and-through silkworm-gut sutures. In the technic developed by Price and continued by himself, Kennedy uses no absorbable suture material in his abdominal wounds. In contrast to the method and results of Kennedy is the equally impressive statement by Baldwin[20] that he performed 16,465 laparotomies without a dehiscence. He used no. 2 chromic catgut throughout in the closure of the layers of peritoneum, muscle, fascia and skin and silkworm gut for stay sutures.

Freeman[21] propounded an explanation for the causation of disruptions which has many adherents. In his opinion the primary cause lies in the inadequate closure of peritoneum with resultant omental protrusion through such a gap. Subsequently, he stated, the omental wedge becomes edematous and with the accompanying serous exudate produces separation of tissues which only needs the strain of coughing or vomiting to precipitate a dehiscence.

Experimentally, Freeman performed laparotomies on 15 dogs, purposely closing the wounds with a tongue of omentum lying between the edges of the layer of split muscle. He reported a swelling of the omental wedge and the production of a lymphlike fluid but no actual disruption of the wound. Certainly, the suture material served its purpose well in these experiments, in which intentional defects in the muscles

19. Kennedy, J. W.: Tragedies of the Abdominal Incision, Am. J. Surg. **25**:512 (Sept.) 1934.

20. Baldwin, J. F.: Disruption of Abdominal Wounds, Am. J. Surg. **25**:7 (July) 1934.

21. Freeman, L.: The Cause of Post-Operative Rupture of Abdominal Incisions, Arch. Surg. **14**:600 (Feb.) 1927.

were present together with the natural activity of the dogs. These results, it seems to me, considerably weaken the tenability of Freeman's theory of the omental wedge. The late Dr. Polak,[22] who had seen 11 disruptions in thirty-five years of practice, believed that the accident began before the patient left the operating table, and he attributed the separation to a straining effort, as from coughing, followed by a break in the peritoneal suture.

BASIC ETIOLOGIC FACTOR

To my mind, the basic etiologic factor in the disruption of wounds rests in the too frequent failure of the suture material, usually catgut, to hold an incised wound of the abdominal wall beyond the point of safety in the healing of the wound. Some cases may have their beginning in the manner described by Polak. I have already mentioned the cases of Ries, who actually heard the snapping of the suture. Many disruptions, I believe, occur later as the result of the inability of the suture—whether it is of inferior quality or of inadequate tensile strength or whether it is too rapidly absorbed or is misused by the operator—to withstand either a single or a long continued assault from an abnormally elevated intra-abdominal pressure during a stormy postoperative period, before the healing wound has acquired enough tensile strength to combat an unusual disruptive force.

In surveying the conclusions of the many surgeons who have investigated the problem of disruption of wounds, one is impressed with the variability in their respective operative technics and with the multiplicity of conflicting "modifications" which they believe will prevent the catastrophe. Kennedy, in recounting his continued success with interrupted through-and-through silkworm-gut sutures, recommended the omission of all absorbable sutures, especially in the closure of wounds in layers. On the other hand, Baldwin performed 16,465 laparotomies without a single dehiscence, using chromic catgut throughout. The latter author particularly emphasized the use of the binder throughout the postoperative period and convalescence, while other operators use it sparingly, or not at all, without sequelae. Another operator was of the opinion that his success might be due to the use of plain catgut throughout, to the exclusion of chromic gut, which is more irritating to the tissues. However, the majority of laparotomies were performed by this operator, with the patient under spinal anesthesia, with its admittedly diminished incidence of complications that tend to increase intra-abdominal pressure. Similarly, the champions of the tension suture were answered by Colp in his report on the use of these sutures in less than a

22. Polak, J. O., in discussion on Horner, D. A.: Postcesarean Bursting of Abdominal Wounds, J. A. M. A. **93**:1126 (Oct. 12) 1929.

dozen cases in a series of 2,750 laparotomies. He credited the elimination of the sutures with the paucity of liquefactive necroses and deep stitch abscesses.

I can think of no better way of discussing the prophylaxis of disruption of wounds than to present a composite statement of the existing opinions of the surgical[11] "Do's and Dont's" in the conduct of an elective laparotomy. Preoperatively, dehydration, malnutrition, anemia, obesity and the diabetic state should be effectively treated when present. At operation, needless to say, one must exercise strict aseptic technic, minimal trauma in the cutting, clamping and retracting of tissues, complete hemostasis and accurate approximation of the severed layers of tissue. Freeman stressed the need for thoroughness in the peritoneal closure, a prime requisite for which is good relaxation. Hence, the necessity of continuing with a sufficient depth of anesthesia to permit closure of the deep layer as well as the more superficial reenforcing layers.

In suturing the posterior sheath and peritoneum care must be taken not to pull the strand too tightly, for it is an easy matter to tear through the transversely running fibers of the tissue. A similar occurrence follows a closure made difficult, if not impossible, by a straining, half-anesthetized patient. Tying knots too tightly or laying down a continuous layer of sutures under too much tension only results in strangulation, necrosis of the tissue and final giving way of the suture. All that is desired is coaptation. Equally destructive is the insecurely tied knot which gives way at the least strain or test of its holding power. Heyd and Lahey have each recommended the suturing of the split muscle, thus obliterating dead space, combating possible infection and adding to the strength of the closure.

The care of suture material is of great import. Dry and brittle catgut should not be used as it comes from the tube, nor should the strand needlessly suffer injury by application of clamps or by faulty laying down of knots. Drains should be used sparingly, especially when left in the peritoneal cavity. The exposure of the wound proper to digestive ferments should be avoided if possible. Tension sutures are most effective when placed with lateral bolt or button support. The circularly tied suture is liable to cut through the tissue enclosed by it and thus do more harm than good. The success established by Kennedy in the sole use of through-and-through nonabsorbable sutures brings up the question of whether the apposition of tissue in mass is not more effective and practical than the closure by anatomic layers, in which multiple small bites of tissue are taken. Absorbable material when used should be of small size and proved quality, and preferably chromicized.

Postoperatively, the binder should be used as a routine. Its benefits overbalance its disadvantages. Everything possible should be done to

combat undue restlessness, vomiting, coughing, hiccup and distention. In this connection one should consider the question of the selection of the anesthetic in cases that appear to promise trouble. Gastric lavages should be performed as indicated by passing the Levine tube transnasally. This method avoids the usual retching and struggle that attend the passage of a regular stomach tube. With the simple method of lavage available, it would seem that autolavage, which demands more effort on the part of the patient, should be discarded. Sutures, especially tension sutures, should not be removed by rote. It would be folly to remove a valuable restraining agent in a patient who is still passing through a turbulent postoperative period. Nonabsorbable tension sutures should remain in situ for from twelve to fourteen days, the time thus extending beyond the period of weakness in the healing of the wound.

CONCLUSION

A consecutive series of 1,560 laparotomies has been studied in an effort to arrive at a clearer understanding of the mechanism of the production of disruption in abdominal wounds. What has been gleaned from this study in the way of figures and facts has been duly recorded and analyzed. I have chosen to dwell on the broader aspects of the problem, elaborating on the phases of the healing of wounds, the usage and fate of catgut and a consideration of intra-abdominal variations in pressure. Only by a study of these fundamental elements in the repair of an incised wound of the abdominal wall could conclusions be reached. Parenthetically, it might be added that too little consideration has been given to the study of intra-abdominal pressure, practically as well as theoretically, for few of the standard texts on physiology even mention the subject.

I believe that most cases of disruption of abdominal wounds represent a failure of the suture line to hold—whether it is due to the suture material or to abuse—in the face of undue intra-abdominal pressure. Without the added factor of excessive abdominal pressure, many inherently weak wounds may escape disruption. The solution lies in the minimizing of the disruptive forces and in the more prevalent use of nonabsorbable, removable sutures, the effect of which is to tide a healing wound over its early period of weakness. I agree with Freeman that the emphasis by some writers on the etiologic importance of age, sex, seasonal incidence, the primary illness and allergic phenomena is merely "begging the question." It is believed that the newly awakened interest in the subject will lead to a revaluation of the present accepted methods of the closure of wounds and to a closer scrutiny of the efficacy of absorbable suture material and of the surgeon's security in using it in the closure of a laparotomy wound.

SO-CALLED "LIVER DEATH"

A CLINICAL AND EXPERIMENTAL STUDY

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AND

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NEW ORLEANS

The conception of disease of the biliary tract which includes in its compass involvements of the liver as well as of the gallbladder is of relatively recent origin. Indeed, it dates from the observation of Reimann of the Lankenau Clinic, in 1917, that hepatitis of some degree is a constant accompaniment of cholecystitis of any degree. That observation was confirmed experimentally by Graham, of St. Louis, in the following year, and since then notable work has been done on the association of disease of the liver with disease of the biliary tract, particularly by Heyd and Martin of New York and by Judd and Walters of the Mayo Clinic, while Riemann's and Graham's further studies have continued the promise of their early investigations. Today, even though all surgeons may not be willing to grant, as many claim, that hepatitis actually precedes cholecystitis in some, if not in all, cases, they accept without question the association of the two diseases, and they comprehend, practically as well as theoretically, that the health and the safety of the patient following operation for biliary tract disease depend largely on the state of the liver.

In 1890, in one of the earliest publications on the subject, Courvoisier reported a mortality of 16 per cent following operations on the biliary tract. In 1934 Heuer[1] reported a mortality of 6.6 per cent in more than 35,000 operations. And Graham,[2] speaking for himself and his associates, recently reported a mortality of 0.4 per cent following simple cholecystectomy and of 2 per cent following operations on the common bile duct. It is not too much to say that this astonishing reduction in the collective and individual surgical mortality is due in no small part to the surgeon's comprehension of the inseparable association of the liver and the gallbladder in cases of disease of the biliary tract, plus, we think it is only fair to add, the commendable habit of modern physicians

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1. Heuer, G. J.: The Factors Leading to Death in Operations upon the Gallbladder and Bile-Ducts, Ann. Surg. **99**:881 (June) 1934.

2. Graham, E. A.: Lowering the Mortality After Operations on the Biliary Tract, Illinois M. J. **60**:196 (Sept.) 1931.

of analyzing their own results, especially their failures. An analysis of this sort, it seems to us, is particularly important in cases of disease of the biliary tract because operation for this particular condition in the majority of cases is done by election, that is, it is done by choice to restore health rather than as an emergency measure to save life.

As soon as the factors of mortality following operations on the biliary tract began to be carefully analyzed, it was promptly realized that they fell—and still fall—into certain definite groupings. The immediate factors, if we may so express ourselves, include hemorrhage, shock and embolism, while the delayed factors include peritonitis and complications of the respiratory tract. But in a certain group of cases, the significance of which Charles Gordon Heyd was apparently the first to comprehend, none of these factors operate. The patients, for the most part, are not desperately ill; the majority of them seem to present an unusually good surgical risk. Many of them die too promptly for the death to be explained on an infectious basis but too late for surgical shock to play any part, while a certain group in whom death is deferred exhibit no clinical evidence of infection or pneumonia. Furthermore, autopsy, the court of last resort in medicine, throws no light on the problem, for it eliminates all the usual causes of postoperative death.

Spurred thereto by his own experience and by his comprehension of the significance of this train of events, Heyd,[3] in continuation of his valuable studies on the liver in its relation to abdominal infection, divided the fatal cases into three general groups in which the course is as follows:

In group 1 the patient is frequently obese and gives a history of long-standing disease of the biliary tract. He is a good risk and has no organic defects that can be demonstrated; cholecystectomy, frequently in combination with appendectomy, is easily done. There is, however, a delayed recovery from the anesthetic; a semicomatose state ensues, which is followed by carphology, subsultus tendinum, coma, and death within from twenty-four to forty-eight hours. Hyperpyrexia is the outstanding symptom in this group.

In group 2 the patient has jaundice, and there is often a history of previous operation on the biliary tract. He is not so satisfactory a risk as the patient in group 1, but he cannot be considered a poor one. Operation, which may range from cholecystostomy to choledochostomy, is not extraordinarily difficult. Convalescence is satisfactory for from thirty-six to forty-eight hours. Then the patient becomes irritable and nervous; there is pronounced and abrupt vasomotor collapse, and death ensues from twenty-four to forty-eight hours later. Hyperpyrexia is again a feature.

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3. Heyd, C. G.: Liver and Its Relation to Chronic Abdominal Infection, Ann. Surg. **79**:55 (Jan.) 1924.

In group 3 the patient exhibits calculous cholangeitis and sometimes pancreatitis, and more rarely there is a pancreatic malignant disease. The seriousness of his condition is realized, but he is properly prepared, and he does not, all things considered, present a bad risk. Operation may be cholecystostomy, choledochostomy and cholecystenterostomy or the creation of an external biliary fistula. Convalescence is satisfactory, or even good, for the first five or six days; the jaundice decreases, and the patient is considered on the road to recovery, when suddenly somnolence ensues, which passes into coma, and death is only a question of time. In this group of cases a deferred renal factor is apparent, beginning as oliguria and frequently progressing to complete anuria, in contrast to the first two groups in which the most striking and dramatic feature of the clinical course is the sharp and progressive elevation of temperature, which, once the upward course has begun, continues without remission until it reaches 106 F. and higher.

Heyd's [3] report, the substance of which we have roughly summarized, was made in 1924, and Cave,[4] two years later, reported 3 cases of a similar nature in a group of 35 in which death followed operation on the biliary tract, all of which seem to belong in group 1. Stanton,[5] in 1930, reported 15 fatal cases of the same type as Heyd's group 1, the data being collected from 100 hospital records which he studied personally. He mentioned Cave's cases, but he seems to have overlooked Heyd's, probably because the title of the paper was misleading. Since then similar cases have been reported and studied by Behrend, Connell, Eiss, Graham, Helwig, Schutz and Kuhn, Petren, Ravdin, Sharples,[6] Wilensky and Colp, and one or two other authors, the total number amounting, in the collective study made by Heuer, to about 95 cases.

But the problem of the so-called "liver death" was soon to assume a wider significance, and not the least interesting feature of it is the manner in which the significance of previous observations on apparently unrelated or at least irrelevant subjects is coming to be realized. Thus in 1927 Furtwaengler, from Clairmont's Clinic in Zurich, introduced an entirely new element into the situation by reporting the case of a young woman who, after an automobile accident, presented precisely the same fatal course as the patients in Heyd's group 3. Helwig and Orr,[7] in

4. Cave, H. W.: Dangers Incident to Cholecystectomy, Ann. Surg. **84**:371 (Sept.) 1926.

5. Stanton, E. M.: Immediate Causes of Death Following Operations on Gallbladder and Ducts, Am. J. Surg. **8**:1026 (May) 1930.

6. Sharples, C. W.: Liver Deaths Following Operation on Biliary Tract, West. J. Surg. **42**:337 (June) 1934.

7. Helwig, F., and Orr, T. G.: Traumatic Necrosis of the Liver with Extensive Retention of Creatinine and High Grade Nephrosis, Arch. Surg. **24**:136 (Jan.) 1932.

1932, reported a similar case, but they, as well as Furtwaengler, overlooked the fact that in Stanton's report just such a case had been reported, although this patient was referable to Heyd's group 1. Stanton gave no postmortem observations, but in Furtwaengler's and in Helwig and Orr's cases autopsy revealed, in addition to the expected traumatic necrosis of the liver, high grade bilateral necrosis of the cortex of both kidneys.

Willard Bartlett Jr.,[8] in an extensive paper on the subject of renal complications of infections of the biliary tract, emphasized the renal factor in these cases. The majority of the cases which he reported are not, in our opinion, entirely germane to this discussion, for the reason that in some instances no operation was done while in others the renal disability was demonstrated before operation. He gave, however, an interesting summary of the particular investigations devoted to this aspect of the problem. In 1911, he pointed out, Clairmont and von Haberer, after reporting 5 cases of renal failure following operation on the biliary tract, 3 of which were fatal, attempted to produce anuria experimentally by ligation of the common bile duct; excretion of dye showed some impairment of function, but the experiments were not successful. In the same year Steinthal noted anuria on the fourth day after operation on the common bile duct; autopsy showed acute tubular degeneration of the kidney. He considered that the anesthetic had precipitated the fatal result, there having been a latent renal insufficiency present as a sequela of hepatic damage. In 1921 Staeheli reported a fatal case in which cholecystectomy and choledochostomy had been performed, but we question whether it has any bearing on the subject, since autopsy revealed arteriosclerosis of the kidneys. A case of oliguria following cholecystectomy, reported by Kehr and mentioned by Staeheli, presents no such extraneous factor and undoubtedly belongs to the group of cases we are discussing. In 1922 Parham and Walters reported instances of several patients dying of renal insufficiency after operation on the biliary tract, and an extended report on the same subject was made by Wilensky and Colp[9] in 1927. It is impossible to mention, let alone summarize, within the confines of this brief paper the work of Rowntree, Snell and Green and many others along both experimental and clinical lines.

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8. Bartlett, W., Jr.: Renal Complications of Biliary Tract Infections, Surg., Gynec. & Obst. **56**:1080 (June) 1933.

9. Wilensky, A. O., and Colp, R.: Relation of Nitrogen Bodies of the Blood to Surgical Problems in Liver and Biliary Tract Diseases: III. Status of Nitrogen Bodies of Blood in Severe Cases of Biliary Tract Disease, and Its Use in Differentiating a Terminal Hepatic and a Terminal Renal Group of Cases, Arch. Surg. **15**:635 (Oct.) 1927.

But there are still other aspects of the problem. Ravdin,[10] writing in 1929 on the subject of vasodepressor substances in the liver after obstruction of the common bile duct, recalled that Ransahoff, in 1908, endeavored to explain the shocklike states which occasionally supervene after such operations. Connell, in 1931 [11] and again in 1934,[12] linked the problem of "liver death" with sudden postoperative death associated with high temperature, cases of which were reported by Gibson, Johnson and Brewer [13] in 1900, Crandon and Ehrenfried [14] in 1912, Moschcowitz [15] in 1916 and Martin [16] in 1928. Reports of 26 such deaths were collected by Cutting [17] in 1931, but he, like all previous writers, endeavored to explain them simply as due to heat strokes, with climatic conditions as the probable underlying cause; the surgical significance of such deaths seems, as we have said, to have been realized first by Connell. Climatic conditions, we might interpolate at this point, would not explain such deaths in New Orleans, where, although long periods of very hot, humid weather are the rule during the summer months, heat stroke as such is an almost unknown accident.

Finally, there is a notable tendency on the part of many recent writers to extend the field of this problem to include not only deaths following operations on the biliary tract and deaths following trauma to the liver but also deaths occurring after such widely different conditions as burns, drug poisoning and intestinal obstruction (Wilensky and Colp). Connell, writing in 1934, definitely retracted the statement which he made in his 1931 paper, that death with hyperpyrexia was noted only after operation on the biliary tract, and we ourselves, as we shall point out later, are in entire accord with his and with Wilensky and Colp's point of view.

It might be well, at this point, to specify the changes which are uniformly noted in these cases at autopsy. In none of them, as we

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10. Ravdin, I. S.: Vasodepressor Substances in the Liver After Obstruction of the Common Duct, Arch. Surg. **18**:2191 (May) 1929.

11. Connell, F. G.: Rapid High-Temperature Deaths Following Biliary-Tract Surgery, Ann. Surg. **94**:363 (Sept.) 1931.

12. Connell, F. G.: Liver Deaths (So-Called), Ann. Surg. **100**:319 (Aug.) 1934.

13. Gibson, C. L.; Johnson, A. B., and Brewer, G. E.: Heat-Stroke as Postoperative Complication, J. A. M. A. **35**:1685 (Dec. 29) 1900.

14. Crandon, L. R. G., and Ehrenfried, A.: Surgical After-Treatment: A Manual of the Conduct of Surgical Convalescence, ed. 2, Philadelphia, W. B. Saunders Company, 1912.

15. Moschcowitz, A. V.: Post-Operative Heat Stroke, Surg., Gynec. & Obst. **23**:443 (Oct.) 1916.

16. Martin, T. M.: Report of Four Cases of Postoperative Heat Stroke, J. Missouri M. A. **25**:305 (July) 1928.

17. Cutting, R. A.: Postoperative Heat Stroke, Am. J. Surg. **13**:624 (Sept.) 1931.

have said, is there any anatomic or infectious explanation for the death. Indeed, in groups 1 and 2 of Heyd's classification the organs are approximately normal, with the exception of the liver, which shows diffuse toxic changes progressing in some cases to degeneration and actual necrosis; usually the only other abnormality is slight congestion of the kidneys. In group 2, on the other hand, just as in the 2 cases of trauma to the liver reported by Furtwaengler and by Helwig and Orr, there is, in addition to these hepatic changes, a marked degree of renal damage, chiefly tubular degeneration which ranges from granular changes to actual necrosis and sequestration of the cells.

In other words, the cases fall into two distinct clinical and histologic groups. In the first group hyperpyrexia and death soon after operation make up the syndrome, while degenerative changes in the liver form the predominant picture at autopsy. In the second group the clinical picture is one of uremia; death is deferred, and there are postmortem changes of a degenerative character in the kidneys as well as in the liver.

One thing that impressed us immediately in our review of the literature on this subject was the wide disparity of the figures, or, more properly, of the impressions, concerning the incidence of so-called "liver death." The majority of authors have mentioned only isolated cases, but Stanton reported 15 which he was able to locate personally from his study of hospital records, and he stated that he would be willing to transfer to this group several other cases set down under other causes of death, while Connell reported 17 in 1931, to which number he added 8 in 1934. Heuer, on the other hand, in spite of his extensive surgical experience, said that he had never seen a case of cholecystitis without jaundice in which the cause of death could not be explained in some other way. The important consideration, of course, is not the exact incidence of the complication but the fact that it does occur and that when it occurs it is almost invariably fatal. A complication of such actual and potential gravity is clearly worthy of serious investigation, and it was with the idea not only of studying our own cases but of seeking some solution for the whole problem that we undertook this study.

CLINICAL DATA

We began our study with an analysis of the last 100 "gallbladder deaths" occurring in the New Orleans Charity Hospital (a separate study of which we shall shortly publish), and we found, to our surprise, that 23 of them, almost 25 per cent, fell into the type under consideration. As a matter of convenience we have chosen to group them as follows:

Group 1.—A. Death within forty-eight hours, with hyperpyrexia; 6 cases: The age range of the patients was from 38 to 68 years, with an

average age of 53 years, and 3 were very obese. All of them gave a history of long-standing infection of the biliary tract, but none of them was acutely ill, and all were regarded as presenting a good surgical risk. None of them had jaundice, but 2 were found at operation to have calculi. In 2 instances the operation was done as an emergency measure several days after admission because of an exacerbation of symptoms, but even these patients had some sort of preoperative preparation. Ether anesthesia was used in 5 cases and spinal anesthesia in 1, and the surgical procedures were evenly divided between cholecystectomy and cholecystostomy. In all cases the clinical course corresponded with Heyd's group 1, death within forty-eight hours with rapidly increasing hyperpyrexia, terminating in an axillary temperature of from 105.2 to 107 F., and an associated rising pulse rate.

B. Death within seventy-two hours, with hyperpyrexia; 5 cases: The age range of the patients was from 24 to 58 years, with an average age of 39 years. Two of the patients were obese, but 2 others had lost considerable weight during their illness, a circumstance which the surgeon who performs operations on the biliary tract is inclined to look on with favor. All of them gave a history of chronic infection of many years' duration; 1 had jaundice, 1 had previously undergone cholecystostomy, and at operation 4 were found to have stones. In 1 case the gallbladder was hydropic, and in another case there was marked hepatitis, but the condition of the liver, as in most reported cases, was unfortunately not stated in the majority of the operative records. One operation was done as an emergency measure immediately after admission; the other patients had more or less adequate preoperative preparation. Ether anesthesia was used in 2 cases, spinal anesthesia in 2 and spinal and ether anesthesia in 1; cholecystectomy was done in 4 cases and cholecystostomy in 1. The clinical course was the same in all cases and suggests Heyd's group 1 classification—a fair recovery or an entirely satisfactory recovery for from twenty-four to forty-eight hours and then hyperpyrexia (105 to 107 F. by axilla) but no other notable symptoms except a rising pulse rate. In all these cases the postoperative carbon dioxide-combining power indicated acidosis, ranging from 24 to 38 volumes per cent. In all the cases in this group and in group 1 A in which autopsy was done the picture was the same, i. e., degenerative changes within the liver and some congestion of the kidneys.

C. Fairly normal course for four or five days, then hyperpyrexia and death within twenty-four hours; 2 cases: Both of the patients in this group, who were respectively 23 and 48 years of age, presented a good risk, and although both gave a typical history of long-standing biliary tract disease, only 1 had jaundice and exhibited stones. Ether

anesthesia was used in 1 case, and ethylene and ether in the other, and in both cholecystectomy and appendectomy were done without difficulty. Convalescence was smooth for the first four or five days; then the clinical course described in groups 1 A and 1 B ensued, with a rapidly mounting temperature (to 106 and 107 F. by axilla) and an associated mounting pulse rate. The deferred death naturally introduces the possibility of peritonitis, but there was no clinical or postmortem evidence of this condition. In both cases, however, some renal factor was apparent at the end; in 1 the patient voided only once within the last twenty-six hours of life, the quantity, unfortunately, not being charted, and in the other also the output could not be measured since the patient voided involuntarily "in small amounts," according to the nurse's notation. In 1 case the carbon dioxide-combining power was 42 volumes per cent, and the nonprotein nitrogen content, previously within normal limits, rose to 50 mg. per hundred cubic centimeters of blood at death. In both cases only partial autopsy was permitted, and a histologic examination of the kidneys was not made, but the marked damage to the liver cells previously described was verified microscopically.

Group 2.—A. Smooth recovery for from five to ten days, then oliguria, progressing to terminal anuria, with symptoms of uremia but an absence of the hyperpyrexia noted in group 1; 4 cases: The age range of the patients was from 32 to 49 years, with an average of 42.4 years. There was the usual history of infection of the gallbladder, and 2 patients had jaundice and exhibited calculi, although again they were not suspected to present a poor risk. One gallbladder was hydropic, and 1 showed a small patch of gangrene. Ether was used in 1 case, ethylene and local infiltration in 1 and spinal anesthesia in 2. Cholecystectomy was done in 2 cases, and cholecystostomy and choledochostomy in 1 each. In all cases there was at first a smooth recovery and then a turn for the worse ensued; oliguria, progressing to anuria, dominated the picture, and death occurred in what amounted to uremic coma. In all cases there was a rise in the amount of nonprotein nitrogen, and the urine showed albumin and casts. In 2 of these cases, as in the similar cases reported by Helwig and Schutz,[18] postoperative rupture of the wound occurred. In the cases in which autopsy was performed parenchymatous degeneration was found in the liver, accompanied by degeneration, progressing to necrosis, of the convoluted tubules of the kidney.

B. Cardiorespiratory collapse in from sixty to ninety-two hours; 3 cases: There was the usual history of long-standing biliary tract disease; the age range of the patients was from 24 to 52 years, with an average

18. Helwig, F., and Schutz, C. B.: A Liver Kidney Syndrome, Surg., Gynec. & Obst. **55**:570 (Nov.) 1932.

age of 44.5 years, and 1 patient was obese. Ether and spinal and splanchnic anesthesia were used, and cholecystectomy was done in all cases. In from sixty to ninety-two hours there occurred marked cardiorespiratory collapse, with clear evidence of vasodepression, and in 1 case there were repeated convulsions. The carbon dioxide-combining power indicated both acidosis and alkalosis (the alkalosis, in our opinion, being explained by the form of therapy employed); it ranged from 22 to 74 volumes per cent, and in the latter case the nonprotein nitrogen content was 74 mg. per hundred cubic centimeters. In another case it was 120 mg. Oliguria was a striking feature in the 2 patients who lived longest. In all of these cases death ensued in from three to six days after collapse had occurred, there being no response to any measures aimed to correct the altered blood chemistry. Postmortem examination, unfortunately, was not permitted in any instance.

When one attempts to analyze these cases it is evident immediately that although clinically and histologically they fall into two distinct groups, there is no obvious common factor to explain the fatality. The age range was very wide, from relative youth to relative old age, so an unsuspected renal lesion is not a reasonable explanation in all cases, for renal lesions of this sort in young persons are most unusual. Death cannot be explained on the basis of anesthesia, for all varieties were used. Some of the patients were obese, but well over half of them were not, and some were thin. The pathologic process was rarely serious enough to make the operation difficult or to cause a bad risk, and although in a few instances technical errors were made, chiefly a leakage of bile, there is not the smallest clinical or autopsy evidence that these accidents played any part in the final catastrophe.

In line with Heyd's suggestion that pancreatic disease is sometimes characterized by this same postoperative syndrome, we investigated the deaths after operation on the pancreas for the last seven years in the Charity Hospital, and while we found no instances of hyperpyrexia we did find 4 cases in which there occurred the sort of deferred death with renal damage which we have been discussing. These cases, for convenience of reference, we shall term group 3.

Group 3.—There were 4 cases in this group. The age range of the patients was from 22 to 62 years. Two patients were obese. Operation was performed in 3 cases as an emergency measure immediately after admission, and 1 patient had previously undergone cholecystostomy, but with one exception all of them, as pancreatitis goes, presented a fairly good risk. Spinal analgesia was used in all cases, and the operations included simple exploration, drainage of the pancreas, cholecystostomy and cholecystectomy and appendectomy. The outstanding feature of the clinical course in all instances was deferred oliguria progressing to anuria and associated with typical changes in

the blood chemistry, chiefly a rise in the amount of nonprotein nitrogen, which in 1 case reached 66 mg. per hundred cubic centimeters of blood and in another, 92 mg. Postmortem examination was done in 2 cases and revealed, in addition to the pancreatic disease, degenerative changes in the liver cells and in the tubules of the kidney paralleling the changes described in the cases in which death followed operation on the biliary tract.

Again, in line with the suggestion of Furtwaengler, Helwig and Orr, and Stanton, that trauma to the liver may produce a similar hepatorenal syndrome, we investigated such deaths, including deaths from gunshot wounds of the liver, which occurred over the last seven years in the Charity Hospital, the same period covered in our study of disease of the biliary tract. The cases which presented this syndrome fall into two distinct classifications, corresponding to groups 1 A and 2 A following operation on the biliary tract, and for convenience of discussion we shall term them groups 4 A and 4 B.

Group 4.—A. Cases following gunshot wounds (3) and following an automobile accident (1): The age range of the patients was from 8 to 32 years, with an average age of 22.3 years. Exploration under ether anesthesia was done immediately in 3 cases and six days after admission in 1 case, after marked jaundice had developed, as in the case reported by Helwig and Orr. In 3 cases the patient died within from twenty-four to thirty-six hours of the injury, with an axillary temperature of from 105.4 to 108.2 F., while in the fourth case hyperpyrexia promptly followed operation, at which, it should be noted, no trace of peritonitis was detected. These cases were all coroner's cases, and autopsy was not permitted within the hospital.

B. Cases in which rupture of the liver occurred as the result of an automobile accident (2): The ages of the patients were 8 and 48 years, respectively. Immediate exploration was done on both, in 1 instance under ethylene anesthesia and in the other under spinal analgesia. The clinical course precisely paralleled that of the patients in group 2 A, who made a smooth recovery immediately following operation on the biliary system but who exhibited deferred uremic symptoms. In 1 case in this group profound jaundice ensued, the icterus index reaching 210. Autopsy in both cases revealed typical degenerative changes within the liver and the kidneys, in 1 instance so extreme as to suggest the pathologic process of acute yellow atrophy.

We were able to locate several other cases following operation on the biliary tract which seemed to fall into one or another of the classifications we have discussed, but we have omitted them from our groupings because other factors which might be open to criticism were present also. In 1 case, for instance, in which operation was performed under spinal analgesia, hemorrhage of a mild—certainly

not of a fatal—degree was an associated phenomenon; death occurred within sixteen hours, with marked hyperpyrexia, and autopsy showed what amounted to acute yellow atrophy of the liver, with tubular degeneration of the kidneys. This patient, it should be added, had previously undergone cholecystostomy. Four other cases were discarded because the element of infection clouded the picture, though in our opinion death occurred too promptly and too typically for it to have played any part in the outcome.

It is evident, then, that after operation on the biliary tract, after operation on the pancreas and after traumatic necrosis of the liver there may occur a typical clinical syndrome in which death occurs promptly, with hyperpyrexia as the outstanding feature, or occurs later, with renal symptoms as the outstanding feature. On the pathologic side, in the first group of cases the postmortem changes are chiefly limited to degenerative changes within the liver, associated with slight congestion of the kidneys, while in the second group the same hepatic changes are present, plus similar degenerative changes within the convoluted tubules of the kidneys. The only marked difference between the deaths following operation on the biliary tract and those following trauma to the liver is, as Helwig and Orr pointed out and as we ourselves have noted, that in the cases in which death follows traumatic necrosis of the liver the degenerative changes within the liver are limited to the traumatized area, whereas in true hepatic disease they are widespread; in both traumatic and pathologic states, however, the damage to the kidneys is widespread.

EXPERIMENTAL DATA

Following this clinical study, and with the clinical syndrome clearly in mind, we endeavored to reproduce in experimental animals the clinical and pathologic processes we had observed in human beings, hoping that some explanation might thus be evolved which would fit all cases, those exhibiting only hepatic lesions and those exhibiting both hepatic and renal lesions. These processes we endeavored to reproduce by the following methods:

1. Traumatic necrosis of the liver.
2. Various types of interference with the hepatic and the portal circulation.
3. Obstruction of the biliary tree.
4. Obstruction of the biliary tree with later release of the obstruction.
5. Intraperitoneal and intravenous injection of extracts made from the livers of animals in which the biliary tree had been obstructed and later released.
6. Injection of the same extracts of animals in which previous damage to the liver had been produced by the use of a carbon tetrachloride mixture.
7. Intraperitoneal injection with the extract of the liver of a patient who died with hyperpyrexia thirty-two hours after cholecystectomy.

8. Implantation of normal liver into the peritoneal cavity, as previously done by Mason, Dragstedt, and Andrews and Hrdina.[19]

9. Intraperitoneal injection of extracts of normal liver, as done by the same authors.

10. Intravenous injection of the same extracts.

It would be well to state at this point the conditions under which all of these experiments were performed. We selected animals which were grossly normal and which had normal renal function as proved by urinalysis and by studies of the blood chemistry. We also measured the twenty-four hour output of urine for several days prior to the experiment to obtain the average for each animal.

All the experiments, furthermore, were conducted under strictly aseptic precautions, and the liver extracts were made under the same conditions. Anesthesia was variously a light ether narcosis or local analgesia for all the experiments except series 2, in which veterinary pentobarbital sodium was used. This anesthetic we found to produce a most satisfactory narcosis when given in the proper dosage, and we observed no evidence of toxicity following its use. Inhalation anesthesia with ether was given in the minimum degree, and while we recognized the possible toxic factor thus introduced, we felt that ether must be used in our experiments if we were actually to parallel the clinical conditions present in these cases.

1. *Traumatic Necrosis of the Liver.*—The abdomen was opened through an upper right rectus incision, and various manual and instrumental methods were employed to traumatize the liver substance without fracture of the capsule. If the capsule was broken and intraperitoneal hemorrhage occurred, the animal was discarded. In all cases there was evidence of more or less shock after the injury, and in a few cases death followed promptly. In the animals which survived there were noted a diminution in the twenty-four hour output of urine, with the appearance of albumin, casts and red blood cells, and an insignificant rise in the amount of blood nitrogen. Within from seven to ten days after the injury these symptoms disappeared, and the animal seemed normal in all respects.

Evidently sufficient hepatic damage cannot be achieved by this method to reproduce the traumatic or pathologic renal damage responsible for the hepatorenal syndrome. Helwig and Schutz,[18] in a series of similar experiments on dogs and rabbits, reported the same difficulties and the same absence of positive renal signs in the animals which survived the immediate period of shock.

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19. Andrews, E., and Hrdina, L.: Cause of Death in Liver Autolysis, Surg., Gynec. & Obst. **52**:61 (Jan.) 1931.

2. *Various Types of Interference with the Hepatic and the Portal Circulation.*—In line with the suggestion made by Ravdin, Behrend and others that "liver deaths" may be due to accidental ligation at operation of some part of the blood supply of the liver, normal or anomalous, we ligated, at various times, the hepatic artery, one branch of the portal vein, one branch of the portal vein and the hepatic artery and both branches of the portal vein. These experiments have given us some very interesting results not germane to this particular discussion, which have been reported in another paper,[19a] but they threw no light on this problem. The animals in which complete occlusion of the portal vein was done at one sitting died promptly, within from thirty minutes to three hours, with the exception of 1 dog which was kept alive for five hours by infusions of dextrose. In all of the animals which survived there was some immediate evidence of shock, but there were no changes in the urinary findings or the blood chemistry to indicate that interference with the portal or the hepatic circulation had reproduced in any degree the pathologic changes of the hepatorenal syndrome. Helwig and Schutz,[18] experimenting with temporary ligation of the hepatic artery in rabbits, achieved positive results in only 1 case. In this instance there resulted an extensive focal coagulation necrosis of the liver and a state of almost complete anuria associated with albumin, casts and red blood cells in the urine and a rise in the nonprotein nitrogen content to 55 mg. per hundred cubic centimeters. These same authors, in another paper[20] written with H. P. Kuhn, mentioned Gunderman's experimental production of uremia by ligation of the hepatic artery.

3. *Obstruction of the Biliary Tree.*—In some animals the common bile duct was ligated and divided, and the distal end was buried; in others the same procedure was combined with cholecystectomy, with the idea of securing a more rapid rise in pressure. In all cases, it should be said, anomalies of the biliary passages were searched for and due account was taken of those found. Jaundice, usually very deep, promptly developed in all the animals so treated, but the urinary findings were practically unaltered, as was the blood chemistry. Such deaths as did occur were quite clearly due to infection, and there was no evidence in any case of the changes in the liver or kidney that we had been seeking to produce.

4. *Obstruction of the Biliary Tree with Later Release of the Obstruction.*—In the animals which survived the obstruction of the biliary tree

19a. Boyce, F. F.; Lampert, R., and McFetridge, E. M.: Occlusion of the Portal Vein: An Experimental Study with Its Clinical Application, J. Lab. & Clin. Med. **20**:935 (June) 1935.

20. Schutz, C. B.; Helwig, F. C., and Kuhn, H. P.: A Contribution to the Study of So-Called Liver Death, J. A. M. A. **99**:633 (Aug. 20) 1932.

just described and in which there was no evidence of infection, the obstruction was continued for from twelve to twenty days. Then the abdomen was reopened and the obstruction was released by the creation of an external biliary fistula. For this purpose we used a specially devised cannula, stopped by a screw, by the removal and reinsertion of which we hoped to be able to release and recreate the obstruction at our pleasure. We were unable to carry out this plan, however, because of the mechanical difficulty of keeping the dogs from pulling at the cannulas or catching them on the wire network of their cages.

In all cases the clinical course was the same following the release of the obstruction. There was a prompt decrease in the jaundice, associated with increasing listlessness, anorexia, (without symptoms related to the gastro-intestinal tract) and death within from seventy-two to ninety-six hours of those animals which were not killed when their state was terminal. There were also noted oliguria which promptly progressed to anuria, together with the appearance of albumin, casts and red blood cells in the urine, and a rise in the amount of nonprotein nitrogen, which in 5 cases was variously 72, 81, 93, 105 and 171 mg. In 3 of these cases (81, 93 and 105 mg.) the estimations were made the day before death, and through a most unfortunate error the final determinations, which we are sure, in the light of the clinical course and the autopsy observations, would have mounted appreciably, were incorrectly made and had to be discarded.

In all cases examination of the abdomen after death showed no evidence of peritonitis. Only faint traces of jaundice were apparent. The liver was greenish and slightly enlarged, and there was no gross evidence of the accumulation of bile.

Histologic examination of the liver and kidneys revealed precisely the same changes noted in human subjects following "liver-kidney deaths." In the liver the periportal areas showed no significant changes; there was no evidence of cholangeitis or biliary stasis, but there were central areas of degeneration, with vacuolation and fragmentation of the nuclei of the liver cells. In some cases there was noted the deposition of a peculiar, homogeneous, red-staining material the nature of which, although not clear from the hematoxylin and eosin stain, was undoubtedly hyaline. In other cases the central area of the liver showed actual necrosis of the liver cells, without significant change in the architecture of the portal fields. In all cases the kidneys showed engorgement of the blood vessels, interstitial hemorrhage and tubular degeneration.

It seems quite clear from this group of experiments that the renal changes found at autopsy in such cases, whether clinical or experimental, are the end-result not of the obstruction of the biliary tract (for we found no such changes in those cases in which only obstruction was

produced) but of the release of the obstruction. Hepatic changes of some degree are, as we have said, the constant accompaniment of all degrees of cholecystitis, but whether the extreme hepatic changes noted in such cases are the result of the original obstruction or of the release of the original obstruction we have not yet determined. There seems no question, however, that they are aggravated by the surgical procedure which releases the obstruction and that the renal changes are positively precipitated by it.

5. *Intraperitoneal and Intravenous Injection of Extracts Made from the Livers of Animals in Which the Biliary Tree Had Been Obstructed and Later Released.*—The livers of the animals so treated which had died or which had been killed when their condition was terminal were removed and run through a small grinding machine, under strict aseptic precautions. The substance thus obtained was extracted with physiologic solution of sodium chloride, with sterile distilled water and with alcohol and the extracts injected into normal animals intraperitoneally and intravenously. The dog given the alcohol extract intravenously died promptly, undoubtedly as the result of alcoholic poisoning, since we discovered that we had miscalculated the lethal dose. All the other dogs survived and showed no clinical or laboratory evidence of pathologic change other than temporary vasodepression following the intravenous injection of the extracts. In the light of the experiments to be described later it may be assumed that these experiments failed because the extracts were not sufficiently concentrated.

6. *Injection of the Same Extracts of Animals in Which Damage to the Liver Had Been Produced Previously by the Administration by Stomach Tube of a Combination of Carbon Tetrachloride, Cottonseed Oil and Alcohol.*—Carbon tetrachloride is a substance which has been proved, experimentally and clinically, to cause various degrees of necrosis of the liver. A few animals died promptly, and those which survived were given intraperitoneal injections of the extracts just described. In a few cases albumin, casts and red blood cells appeared in the urine, accompanied by an insignificant rise in the amount of nonprotein nitrogen, but in no case was the damage terminal or permanent. The conclusion is either that we did not damage the liver sufficiently to bring about the first stage of the hepatorenal syndrome or that we allowed so long a time to elapse between the production of the hepatic damage and the injection of the liver extract that full regeneration of the damaged liver cells had occurred. The inadequate concentration of the extracts is another factor to be considered.

7. *Intraperitoneal Injection of the Extract of the Liver of a Patient Who Died with Hyperpyrexia Thirty-Two Hours After Operation on the Biliary Tract.*—The patient, a woman, aged 57, submitted to

cholecystectomy for cholelithiasis and died promptly after operation with the typical syndrome of hyperpyrexia of Heyd's group 1 and our own group 1 A. At autopsy peritonitis was ruled out, as were hemorrhage, leakage of bile, embolism and pneumonia. A stone, undetected at operation, was found in the common bile duct, but it clearly played no part in the fatal outcome.

The liver was ground and extracted with physiologic solution of sodium chloride, with sterile distilled water and with alcohol, and each extract was injected into a separate dog intraperitoneally, the dosage being doubled each succeeding day. All the dogs died within seventy-two hours of the first injection, and all exhibited casts, albumin and red blood cells in the urine. This experiment was one of the first to be performed, and since its full significance was not then realized no determinations of the blood chemistry were made, which is, of course, a serious defect in our chain of evidence.

Autopsy on the dog given injections of the alcohol extract showed no significant changes, but in the dogs given injections of the saline and the watery extract there was marked parenchymatous degeneration of the liver cells, with similar degenerative changes in the convoluted tubules of the kidneys, as well as marked engorgement of the renal blood vessels and interstitial hemorrhage. Since this is precisely the histologic picture exhibited by the patients who died with the so-called hepatorenal syndrome, there seems no question that there was present in the extract made from the liver of the patient who died a "liver death" after operation on the biliary tract some substance capable of reproducing the histologic picture in experimental animals. There also seems no doubt, since only the saline and the watery extract reproduced it, that the substance, whatever its nature may prove to be, is water-soluble. We feel certain, as we have said, that we could have reproduced the same picture with the extracts made from the livers of the dogs which died after release of their experimental biliary obstruction had we made them in sufficient concentration.

8. *Implantation of Normal Liver into the Peritoneal Cavity.*—This experiment was previously carried out by Mason, Dragstedt, and Andrews and Hrdina.[19] We have repeated it in order that we might prove to our own satisfaction that the introduction of normal liver into the peritoneal cavity, while it causes the autolytic peritonitis described by the aforementioned authors, presents no parallel to the type of "liver death" in which damaged liver is the source of the lethal substance elaborated. We were able to duplicate their findings in all regards. We made careful studies of the temperature of these animals, hoping that we might obtain in this fashion some clue to the hyperpyrexia of Heyd's and of our own group 1, for which, as yet, we had

no explanation, but in no case was hyperpyrexia noted and in only 1 instance did the rectal temperature reach 105 F.

9. *Intraperitoneal Injection of Normal Liver.*—This experiment was also carried out by Mason, Dragstedt and Andrews and Hrdina. All of their dogs died within from seven to eighteen hours, with autolytic peritonitis. We were not able to duplicate these results, although we carefully reproduced the conditions of their experiments and used incubated, concentrated extracts of normal liver made up according to their directions. All the dogs which we used for this experiment lived and showed no reaction of any sort, temporary or permanent, other than a slight immediate reaction after the injection, which is to be expected. For our own purposes this series of experiments proved again that normal liver and diseased liver do not cause the same pathologic processes, but why we failed to reproduce the lethal results of the other experimenters we are at a loss to comprehend.

10. *Intravenous Injection of the Extracts of Normal Liver.*—These injections produced no clinical or laboratory results of any sort and need no detailed discussion.

To summarize, then, the results of these various experiments, we may say that traumatic necrosis of the liver to a sublethal degree, interference with the hepatic and the portal blood supply to the same degree and obstruction of the biliary tree failed to produce in experimental animals the hepatorenal syndrome seen in human patients after operation on the biliary tract. The experimental production of autolytic peritonitis, as well as the intraperitoneal and the intravenous injection of the extracts of normal liver, proved irrelevant to our purpose. On the other hand, the release of experimentally produced obstruction promptly initiated a clinical course and a postmortem picture, gross and histologic, precisely similar to the clinical and postmortem picture observed in human subjects who die under the same conditions after operation on the biliary tract. Injection of various extracts made from the livers of these animals failed to reproduce the same picture in other animals, chiefly, we feel now, because of errors in concentration of the extract. However, the same picture was reproduced by the injection of the saline and the watery extract of the liver of a human patient who died suddenly after cholecystectomy, with hyperpyrexia.

COMMENT

The conclusions to be drawn from this clinical and experimental study seem to us to be very clear and may be summarized as follows:

There is in all cases of biliary tract disease an associated hepatic state. Whether it is antecedent or consequent is still a matter of dispute and makes no special difference in this discussion. It can, however,

in certain cases be of enormous significance. If it is unaltered by the onward march of the disease, a hypothesis which is scarcely tenable, or if it is unaltered by operation, it will have no fatal consequences. The moment, however, it is altered by surgical release of the obstruction, however slight and trivial the obstruction may have seemed, it becomes progressively more severe, which brings one sharply up against the fact that the very means adopted to relieve the disease may kill the host, a situation analogous to operation for intestinal obstruction, for instance, in which the release of the obstruction often permits a fatal onrush of toxic intestinal contents into the still undamaged area of the bowel. This state of affairs is over and above all the other concomitants of operation, the risk of anesthesia, surgical trauma, changes of temperature and the anatomic changes consequent on the removal of the gallbladder from the bed of the liver.

One or two of these considerations must be mentioned in more detail. The effect of the anesthetic, for instance, quite aside from anything else, depends on the agent employed and on the amount of hepatic damage already present. The work of Rosenthal, Bourne and others, chiefly with dye tests, has shown that ether causes a definite although transitory impairment of hepatic function, rarely lasting longer than twenty-four hours, while Colunumal and Ascoli, Kehr, von Haberer and Stahler, Wilensky and Colp and others have pointed out that in biliary disease, particularly when there is associated jaundice, hepatic and renal damage already exists which cannot fail to be intensified by the trauma of the anesthetic. On the other hand, cogent as these arguments are, they do not hold in all cases, for a large proportion of the "liver deaths" reported followed operations performed under other than ether narcosis.

Surgical trauma needs little discussion, for it is clear that the unavoidable trauma of a skilled surgeon will be many times increased by the inexpert manipulations of a less skilled one. From the anatomic standpoint, Heyd [21] pointed out that, quite aside from the change in hydrostatics, the effect of any cholecystectomy is to leave in the liver a denuded fossa of varying extent, which is capable of transudation and absorption of protein. Furthermore, even in cases in which there is no obstruction the mere drainage of the gallbladder, let alone its removal, brings about, through changes in pressure, a reactionary hyperemia, and the operation of the ordinary laws of physics makes this reaction even more acute and more extensive in cases of obstruction.

Another point which cannot be ignored is that even the slight exposure attendant on merely opening the abdomen reduces the tem-

21. Heyd, C. G.: "Liver Deaths" in Surgery of Gallbladder. J. A. M. A. **97:** 1847 (Dec. 19) 1931.

perature of the liver, as Crile has shown, from 1.5 to 3 degrees. This same investigator has also shown that there is a decrease in the chemical activity of this organ by some 10 per cent for every drop in temperature of 1 degree and that if disease has reduced its activity by as much as 10 per cent a reduction of temperature by even 1 degree is likely to result fatally.

We need scarcely discuss the point that if these things are true of the normal liver they are even more likely to be true of the subnormal or abnormal liver. Furthermore, no absolutely satisfactory test as yet exists by which the surgeon can measure the degree of hepatic function. The most accurate test available still gives only approximate results. The amount of damage to the liver, as we know, bears no special relation to the amount of pathologic change in the biliary tract, indeed, it may be entirely inverse to it. In advanced cases of disease of the biliary tract the surgeon suspects a high degree of hepatic damage, even if he cannot estimate it exactly, but in the type of cases we are investigating, in most of which there is an absolutely or a relatively good risk, he has little help from the laboratory. In other words, the surgeon knows, as a matter of general knowledge, that some degree of hepatic damage is always associated with any degree of damage to the biliary tract, but whether it is extreme or minimal he has no accurate way of determining.

So far, then, the chain of events is this: The patient with or without gross obstruction of the biliary tree has some degree of hepatic damage, but it is not incompatible with life. So long as the liver is put to no strain and stress other than that of ordinary living, to which it has accustomed itself, so to speak, it is quite capable of carrying on. But when operation is undertaken, an entirely different complexion is put on the matter. Even in the most favorable cases there are introduced, alone or in combination, the factors we have just been discussing, the strain of the anesthetic, the trauma of surgical manipulation, the drop in intra-abdominal temperature and the changes in intrahepatic and biliary pressure. The result is that a liver which is already the seat of a pathologic process is unable to cope with the added strain, and its function promptly fails. It is already the seat of a permanent and more or less marked toxic reaction, and it cannot fulfil the further demands on its economy as could a normal organ. The toxic substances which reach it in the course of normal body metabolism are thrown off undetoxified, and the liver cells, as they become increasingly unable to fulfil their function, undergo some necrotic change, partly because of failing function and partly because of the changes in intrahepatic pressure brought about by operation. The circulation, therefore, is filled both with the undetoxified substances which the liver has been unable

to handle and with, we postulate, some toxic substance cast off by its own necrosed cells.

The next assumption is an entirely logical one. The kidney is, after the liver, the great detoxifying organ of the body, and once the liver has failed in function, the kidney, purely as a matter of physiology, must take up its work. But the difference is that while the margin of safety in the liver is enormous, the margin of safety in the kidney is slight. The kidney is not fitted by nature, as is the liver, to detoxify, either quantitatively or qualitatively, the normal products of body metabolism, let alone, in addition, the toxic substances elaborated by the damaged liver cells. The result is that it promptly breaks down, and an overwhelming toxemia is the natural consequence.

The physiology of the kidneys is too well established to need repetition here, but one point should be emphasized, i. e., that toxic products are excreted through the convoluted tubules. This has been established experimentally by the use of salts foreign to the blood, and the same process would be operative with the toxic products of necrosed liver cells. The pathologic result, so to speak, is just what one would expect in the light of those facts. The sensitive epithelium of the convoluted tubules shows changes ranging all the way from slight granular changes to complete necrosis and sequestration, while the glomeruli remain practically undamaged. The clinical phenomenon is, as we have noted, oliguria which progresses to anuria, in spite of the undiminished if not actually increased fluid intake always forced on the patient in an endeavor to correct his perverted blood chemistry.

Our personal opinion, which we think is substantiated by the clinical and experimental facts we have stated, is that the hepatic damage always precedes the renal damage and that if the patient who dies promptly with hyperpyrexia and shows hepatic changes at postmortem examination could be kept alive long enough he too would show precisely the same clinical and postmortem renal changes as does the patient who dies later. The patient who dies promptly undoubtedly has a more overwhelming toxemia, perhaps qualitative but more probably quantitative, than the patient who dies after cardiorespiratory collapse (group 2 B), while death which occurs after from ten to twenty days is best explained in the light of our present knowledge as due to protein intoxication in contrast to the probable anaphylactic reaction of early death with high temperature. The patient has a preexisting hepatic damage; small amounts of the toxic substance elaborated in the damaged liver cells are released into his system, but he is sensitive to the substance and can handle it. He cannot, however, handle the massive amounts released postoperatively. Furthermore, even though his damaged liver can stand the strain and stress of ordinary life, it cannot withstand the

added strain and stress of surgical trauma and its concomitants, and his kidneys, especially if they are in any way prediseased, as they so often are in persons of advancing years, have no margin of reserve.

We make no claim for originality for this theory, except in certain details, but we do claim that we have established it in some regards by experimental proof which has not hitherto been adduced, and we have carried it, we believe, slightly further than have the other investigators who have supported it. A brief review of the various other theories which have been advanced to explain the problem of "liver deaths" might be profitable at this point:

Heyd, the first to consider "liver death" as a distinct postoperative entity in disease of the biliary tract, expressed the belief that in the group 1 type of death (with rapidly increasing hyperpyrexia) certain deleterious substances are released at operation, the whole mechanism suggesting complete and rapid cessation of hepatic function, and that in the second group (death with hyperpyrexia within from forty-eight to seventy-two hours), there is a toxic inundation of the system and direct poisoning of the liver cells, again with cessation of hepatic function. In the third group (deferred death with renal symptoms), according to him, death is due to throwing on an already damaged liver the burden of detoxifying an increment of deleterious products released by operation, the result being a progressive increase of hepatic dysfunction.

Heyd also advanced the theory, which is purely speculative, as he himself admitted, that in the group of cases in which pancreatic disease is a factor the underlying cause of death may be some pancreatic toxemia. Aside from the fact that the existence of a pancreatic toxin has never been demonstrated, this theory in no way explains the cases in his own group 1 and group 2, in which pancreatitis plays no part. His theory of hepatic dysfunction is, of course, the same in its essence as the majority of the theories since advanced to explain these deaths; it does not, however, go far enough to include the renal aspect, nor does it explain the details of the mechanism.

Cave's idea is much the same, i. e., that the sudden liberation of toxins from the liver or of pieces of chemically altered liver cells into the general circulation is responsible for the catastrophe. He mentioned as other possible causes the stirring up of infected bile in the intrahepatic ducts as the result of operative manipulation and the partial cessation of hepatic function caused by the shock of the actual removal of the external biliary viscus from its bed, with the resulting exposure of the surface of the liver. The latter considerations, of course, are operative in fatal and nonfatal cases alike, and the toxic theory, while it is correct in its fundamental conception, does not go far enough.

Ravdin and Behrend suggested that the syndrome may be due to the accidental ligation of the hepatic artery, which is anomalously placed in a high percentage of cases, as high, according to some authorities, as 33 per cent. Even granting that any interference with its blood supply is naturally likely to affect the liver in some way, this theory does not explain those cases in which anomalies of the vascular supply are absent, as has been proved by autopsy in many reported cases, while our own experiments and those of Helwig and Schutz seem definitely to disprove it. Such a theory, furthermore, does not explain the cases of traumatic necrosis of the liver and kidney reported by Furtwaengler, Helwig and Orr and ourselves, in which the same syndrome is present but in which an anomalous blood supply could play no possible part.

Guthrie and Robertson [22] suggested that the administration of ether may be the cause of the "liver deaths" and pointed out that in their own clinic, in which ether is never used in abdominal operations, no fatality in 434 operations on the biliary tract seems to fall into Heyd's group 1. The first objection to that theory is that in many reported cases ether anesthesia was not used. The second is that in our own opinion at least 1 case which they report in detail in their series of early deaths after operation on the biliary tract and which they themselves set down as due to hepatic failure and classify as Heyd's group 3, seems to us to fall into group 1: A woman, 24 years old, died suddenly, with high temperature, thirty-three hours after cholecystectomy and exploration of the common bile duct; there was pronounced cardiorespiratory collapse immediately before death. Two other cases described by the same authors seem to us, in the absence of complete details, to be possible examples of deferred deaths with uremic symptoms, while they themselves classify 2 other cases, described in detail, as probable examples of Heyd's group 3. Postmortem observations are not given in any of these cases, and discussion of them, therefore, is little more than speculative.

Stanton mentioned Crile's suggestion of a relationship between the thyroid, the adrenals and the liver as worthy of consideration, and he mentioned also the suggestions of various surgeons with whom he discussed the condition, which include injury to the nervous mechanism of the liver and the absorption of toxic bile or of diseased or chemically altered liver cells. Connell expressed the belief that the mechanism of death is some chemical or metabolic reaction of an unknown nature.

Walters and Parham emphasized the difference between hepatic and renal insufficiency in these cases in a report published in 1922,

22. Guthrie, D., and Robertson, H.: Is Ether a Cause of "Liver Death" Following Gallbladder Surgery? Guthrie Clin. Bull. **2**:11 (July) 1932.

before the full significance of the syndrome was realized, but in the light of more recent work, and particularly in the light of our own experimental studies, we cannot accept this distinction. Willard Barlett Jr., seemingly inclined to emphasize the same distinction, stated that there is no evidence that hepatic cell damage serious enough to cause renal damage must precede the pathologic process in the kidneys, his idea being that infection of the bile passage and not some toxic phenomenon is the cause of the nephritis. We are speaking, as we have already pointed out, of cases which for the most part are not parallel, but we cannot agree with his theory even for the comparable cases for several reasons. In the first place, we do not think that it is logical to disregard the hepatic factor which is apparent to some degree in all cases of biliary tract disease. In the second place, all cases in which the hepatorenal syndrome is present are not associated with infection of the bile passages. Stanton, who was at first inclined to the theory of infection, discarded it for just that reason, especially after he had encountered the case of traumatic necrosis of the liver in which the same syndrome was noted but in which infection could not possibly have played any part. Finally, if infection of the bile passages were the cause of this syndrome, the nephritic factor would be apparent in more cases after operation, instead of which its incidence, in proportion to that of infection, is really quite small.

Ransahoff, noting the shocklike states which sometimes supervene immediately after operations on the common bile duct, advanced the theory that the cause is a sudden stretching or pulling forward of the structures in the gastrohepatic omentum, with consequent constriction of the portal vein, but this, as Ravdin pointed out, is not an adequate explanation; it does not explain cases of deferred death, nor does it explain those cases in which the common bile duct is not handled. Ravdin himself advanced the vasodepressor theory, which, it must be admitted, has much to be said for it. Vincent and Sheen, he pointed out, as early as 1903 were able to extract from the liver a depressor substance, and he himself, working along this line, was able, after experimental ligation of the common bile duct, to obtain a substance containing histamine and choline, both of which are notoriously vasodepressant in action. His theory is that an overwhelming amount of this substance is suddenly released at operation or, as Helwig and Orr pointed out, after trauma of the liver. Theoretically, the latter authors added, such a substance might cause sufficient vasodilatation to produce renal damage, but Ravdin himself, so far as we can gather, does not draw that conclusion. Again, it has been proved that the amount of depressor substances in jaundiced hepatic tissue is considerably in excess of the amount in unjaundiced tissue, so the

explanation, it seems to us, is not particularly helpful for those cases which really furnish our chief problem, those in which the disease of the biliary tract is not of extreme degree. We have no doubt that Ravdin's theory is correct, but we do not believe, nor, for that matter, does Ravdin himself claim, that vasodepression is the chief cause or the only cause of the hepatorenal syndrome.

Wilensky advanced the idea that the initial lesion in the biliary tract produces a primary effect on the hepatic cells and a secondary effect on the renal apparatus, it being highly probable that in hepatic disease some of the catabolic products of liver metabolism and the end-products dependent on its injury are not without effect on the kidney. Such an explanation covers the picture of uremia associated with the so-called cholemia or hepatic toxemia, but it does not provide, as does our theory, for the successive steps of the injury extending from the biliary tract into the liver cells and thence into the convoluted tubules of the kidneys. Basically it is correct, but again details are lacking.

Furtwaengler believed that his patient, in whom bilateral necrosis of the cortices of the kidneys followed traumatic necrosis of the liver, had a latent tendency to vascular spasm due to some nervous disposition, and that the necrosis of the renal cortices resulted from ischemia produced by some hypothetic chemical toxin circulating in the blood and rising from hepatic decomposition. We see no particular necessity for introducing the idea of a tendency to vascular spasm; indeed, we think it highly improbable that it could be a common factor in all cases of trauma, let alone in the similar cases following operation on the biliary tract, which we, together with Stanton and with Helwig and Orr, believe to belong in the same pathologic group. Helwig and Orr properly discard the theory that jaundice is responsible. Undoubtedly it can cause a certain degree of renal damage, but, as they pointed out, in their case the picture was not one of true biliary nephrosis, while jaundice was no part of the picture in Furtwaengler's case, and it was noted in only 1 of the 6 cases of trauma to the liver which we ourselves are reporting.

The explanation for the hepatorenal syndrome advanced by Helwig and his co-workers, Schutz, Kuhn and Orr, is that some potent poison is elaborated in the necrotic hepatic tissue which has a specific effect on the renal parenchyma, causing progressive degeneration and sometimes complete necrosis of the tubular epithelium. They believe that the specific action on the kidney is proved by the fact that other highly specialized viscera, which invariably show the same type of parenchymatous degeneration in the presence of circulating toxins, do not show it in this condition. With the premise of this theory, that some toxic substance is elaborated by the damaged liver cells, we are in complete

agreement. We do not believe, however, that it is necessary or even logical to postulate a specific action on the kidney. The kidney is the normal organ of excretion. Foreign proteins are excreted through its convoluted tubules, and in the so-called hepatorenal syndrome parenchymatous degeneration occurs in the tubules and nowhere else. It is unnecessary, in our opinion, to seek for a more complicated explanation. The kidney, we believe, suffers not through any specific action of the toxic substance released by the liver cells but simply in the fulfilment of its normal physiologic function, or, to speak more accurately, in the fulfilment of the abnormal duty suddenly placed on it. The possible effect of the toxin on the kidney tissue must also be taken into account.

We have already intimated that with the passage of time it has been suggested by various writers on the subject that this particular syndrome, either prompt or somewhat deferred death with hyperpyrexia, or deferred death with uremic symptoms, is not limited to operation on the biliary tract. Heyd, who first described this syndrome, classified in a special group the cases in which there was no biliary tract disease but usually pancreatic disease or more rarely gastro-intestinal disease and in which the same postoperative syndrome was apparent. We have already substantiated his cases of pancreatic involvement with 4 cases from our own records. The traumatic cases reported by Furtwaengler, Stanton and Helwig and Orr we have been able to parallel with a group of 6 cases following gunshot wounds or traumatic injuries of the liver. Wilensky is of the opinion that the same syndrome may be apparent in cases of burns, drug poisoning and high intestinal obstruction. The case of apiol (parsley camphor) poisoning reported by Thiers which terminated in death with the hepatorenal syndrome seems an instance of this sort. Helwig and Schutz reported in their group of 6 cases 1 in which the uremic syndrome was apparent eleven weeks after an operation for carcinoma of the breast, and they mentioned a case reported by LeNoir in which an operation for gastric ulcer terminated in death, with the hepatorenal syndrome.

Heuer, who denied any personal experience after operation on the biliary tract with cases falling into Heyd's and our own group 1, mentioned a case in which splenectomy was performed for supposed Banti's disease, in which later the condition proved to be either reticulosarcoma or Hodgkin's disease and in which death with hyperpyrexia occurred within twenty-four hours. We recently encountered a somewhat similar case in our own service. The patient, a Negress, who was regarded as presenting an excellent surgical risk, was submitted to resection of the cecum for chronic typhlitis. She died within seventy-two hours with an axillary temperature of 105.2 F. and a nonprotein nitrogen content of 76 mg., in contrast to a preoperative level of 29 mg. Autopsy

eliminated the possibility of peritonitis and other surgical complications and revealed the hepatorenal changes typical of the syndrome we are discussing. In another case of carcinoma of the pancreas with metastasis to the liver the same changes were noted.

Connell, writing in 1931, stated that the syndrome of sudden death with hyperpyrexia, was not apparent after any operation other than that on the biliary tract, but he withdrew the observation, as we have stated, in his last paper on the subject, and mentioned its occurrence following operations for ovarian cyst, uterine fibroid tumors, chronic appendicitis, ventral hernia and fracture of the skull. It is true that in at least one of those patients there was a former operation for biliary tract disease, and it is also true that cranial injuries are notoriously prone to produce high temperature reactions, but the list of cases, even with those exceptions, is impressive. Furthermore, in the 26 cases of postoperative heat stroke reports of which were collected by Cutting, only a few, as Connell pointed out, followed operation on the biliary tract, and there is little doubt that most of them, in view of the present knowledge would fall into the category we are discussing.

In the light of these suggestions we studied the results of a series of autopsies, casually selected and all of recent date, performed in cases of burns, intestinal obstruction and disease of the thyroid, and we were struck with the parallelism, which we noted again and again, between those cases and the cases in which death followed hyperpyrexia and the hepatorenal symptoms after operation on the biliary tract. In most instances, too, when the clinical course was typical, the postmortem changes were also typical, necrotic changes in the liver, with or without similar changes in the convoluted tubules of the kidneys, depending on how long the patient lived after operation or injury. We have no doubt that similar sudden deaths, with high temperature, occurring in cases of appendicitis and of kindred conditions might well be included, but we have not chosen to consider them because the element of infection naturally distorts and confuses the picture.

We are particularly impressed with the occurrence of the hepatorenal syndrome in cases of disease of the thyroid. The hepatic factor, of course, is no new thing, but we are not aware that the renal aspect has heretofore been particularly emphasized. Weller,[23] for instance, in 44 autopsies in cases of hyperthyroidism, found evidence of marked hepatitis in 22 and moderate hepatitis in 16, while in only 6 cases in the series was the liver normal. In a control series of other conditions he noted precisely reverse conditions, i. e., 30 cases in which there was no evidence of hepatic involvement, 13 with slight involvement and only

23. Weller, C. V.: Hepatic Lesions Associated with Exophthalmic Goiter, Tr. A. Am. Physicians **45**:71, 1931.

1 case with marked involvement. Rowe,[24] studying nearly 4,000 cases of various diseases, found the incidence of hepatic involvement, even including figures which he describes as "heavily over-weighted," to be at most 10.91 per cent, whereas in 644 cases of hyperthyroidism the incidence of hepatic disease was 22.44 per cent, nearly twice as great. Kerr and Rusk,[25] in 1922, reported a case of hyperthyroidism in which autopsy revealed what amounted to acute yellow atrophy of the liver, with marked parenchymatous changes in both the liver and the kidneys, and in a paper written in 1930 Kerr [26] mentioned several somewhat similar cases observed since then.

The most indubitable proof, however, has been advanced experimentally by Hashimoto,[27] in 1921, his experiments being confirmed by Goodpasture in the following year. They fed albino rats with thyroid substance in an endeavor to reproduce the myocardiac changes of disease of the thyroid observed in human patients, and they reproduced not only those changes but also parenchymatous changes in the liver and in the convoluted tubules of the kidneys.

One wonders, in the face of this evidence, whether this syndrome is not considerably more frequent than is realized. Crisp,[28] for instance, reported from the Mayo Clinic a case of "secondary shock" which occurred twelve hours after resection of the rectum for a malignant condition, too early for peritonitis and too late for surgical or anesthetic shock. The temperature rose to 105.4 F., and there were all the classic signs of extreme toxicity; renal function, however, was unimpaired, and recovery followed. Keith, discussing this case, mentioned three personal cases in which exactly the same syndrome developed, with a fatal termination each time. The liver is not described, but autopsy showed cloudy swelling of the kidneys. Keith introduced the idea that perhaps the syndrome is due to the products of anaerobic bacteria, but one wonders whether his cases, as well as Crisp's case, might not be still other instances of the hepatorenal syndrome.

CONCLUSIONS

Our experimental study has not yet progressed to the point at which we feel that we can make suggestions of any value to prevent

24. Rowe, A. W.: Endocrine Studies: XXXV. Association of Hepatic Dysfunction with Thyroid Failure, Endocrinology **17**:1 (Jan.-Feb.) 1933.

25. Kerr, W. J., and Rusk, G. Y.: Acute Yellow Atrophy Associated with Hyperthyroidism, M. Clin. North America **6**:445 (Sept.) 1922.

26. Kerr, W. J.: Necrosis of Heart and Liver in Thyrotoxicosis, with Some Notes on Possible Changes in Other Organs, Northwest Med. **29**:430 (Sept.) 1930.

27. Hashimoto, H.: Heart in Experimental Hyperthyroidism with Special Reference to Its Histology, Endocrinology **5**:579 (Sept.) 1921.

28. Crisp, N. W.: Toxemia Producing Shock After Operation, Proc. Staff Meet., Mayo Clin. **5**:128 (May 7) 1930.

the distressing catastrophe of "liver death." The most important consideration, it seems to us, lies in Graham's rather casually uttered statement that there is little doubt that the patient with a damaged liver presents a questionable risk not only for operations on the biliary tract but for any operation, no matter how trivial it may be. Other writers, notably Shearer [29] within the last year, have made the same point, and that warning, taken at its face value, will mean, for all practical purposes, a surgical revolution. It will mean that there will be no more "simple surgery." It will mean, particularly, that the surgeon who proposes to perform operations on the biliary tract not only must remember that hepatic disease of some degree is an invariable concomitant of biliary tract disease of any degree but must regard all his candidates for such operations as presenting potentially poor risks, regardless of how incongruous their inclusion in such a category may seem. It means, to go further, that all candidates for any operation must be studied from the standpoint of hepatic function and that the ninety and nine must be discommoded and inconvenienced to rescue the one who may otherwise be lost.

At present, however, no test is available which gives anything but an approximate idea of the efficiency of hepatic function. The details of such tests are no part of this paper, but it seems nothing but fair to call attention to the results achieved by Graham,[30] the best on record, we would say, and certainly worthy of emulation. Using iso-iodeikon and taking a 50 per cent retention as an arbitrary standard of safety for operation without elaborate preparation, he was able to reduce his mortality in simple cholecystectomy from 6 per cent in 216 cases to 0.4 per cent in 224 cases, while in operations on the common bile duct his mortality fell from 7.7 to 2 per cent. Regardless of how inaccurate a test may be, it is worthy of routine use if it can produce results such as those.

In the same connection we consider Wilensky's suggestion of real value, that hepatic function be estimated in the light of renal function and that evidence of renal insufficiency in cholelithiasis and kindred diseases be regarded as presumptive evidence of hepatic insufficiency.

Preoperative preparation, as Shearer in particular pointed out, seems as wise for the patient who apparently presents a good risk as for the patient who frankly presents a poor risk. It should include, according to the indications, a diet high in carbohydrates, fluids by all routes, dextrose as necessary, orally and intravenously, and calcium,

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29. Shearer, J. P.: Mortality Following Gallbladder Surgery, Ann. Surg. **98**: 1114 (Dec.) 1933.

30. Graham, E. A.: Estimating Risk of Operations on Biliary Tract by Testing Excretory Function of Liver, Radiology **21**:191 (Aug.) 1933.

not so much for the control of possible hemorrhage as because Lamson, Minot and Robbins have shown (Graham) that hepatic damage caused by carbon tetrachloride is repaired more rapidly under this form of therapy.

It seems scarcely necessary to say that the anesthetic should be chosen with judgement and that ether should positively be avoided in the presence of actual or presumptive hepatic damage. Manipulations should be conducted with as little trauma as possible. Unnecessary and prolonged exposure of viscera should be regarded as definitely harmful. The suggestion of Crile that diathermy be used in abdominal operations to maintain body temperature has not been generally adopted, but occasional reports, most recently from the clinic of Sobre-Casas in Buenos Aires, testify to its worth (Eiss [31]).

Gradual decompression of the obstructed biliary tree, in the light of clinical evidence and of our own experimental evidence that it is not the obstruction but the release of the obstruction which does the damage, seems worthy of adoption. Culligan recently described a method which involves drainage of small quantities of bile, from 6 to 10 cc., at intervals of thirty minutes for the first four days after operation, at the end of which time it is assumed that the liver has been able to readjust itself gradually to the new pressure so that no sudden enlargement of the capillaries of the portal system can occur. He gave no statistics but stated that since he adopted this plan he had no case of either postoperative hemorrhage or so-called hepatic insufficiency. The method implies personal nursing, which would make its routine use difficult in public institutions or, for that matter, in many private ones without special nursing, but it is clearly a wise precaution.

Mann, as Helwig and Schutz mentioned, suggested that it may actually prove inadvisable to suture the liver after cholecystectomy, for fear of bringing about sufficient necrosis of liver cells to release toxic products into the circulation in the light of his own demonstration that the most profound acute and chronic changes are found in the hepatic parenchyma in the region of the gallbladder, this seems a perfectly logical idea. More than one writer has suggested, too, that the patient's interests may be better served by cholecystostomy than by cholecystectomy, and while the practice may be open to objection on many counts, it does not seem, as Walton Martin [32] pointed out in 1927, to predispose to hepatitis. In a valuable discussion of the relation between hepatitis and cholecystitis he made the point that in the era when

31. Eiss, S.: Conservation of Hepatic Function in Gallbladder Operations, Ann. Surg. **98**:348 (Sept.) 1933.

32. Martin, W.: Hepatitis and Its Relation to Cholecystitis, Ann. Surg. **85**: 535 (April) 1927.

cholecystostomy was the common practice no report was ever made in which the retention of even a grossly infected, drained gallbladder set up chronic hepatitis.

Finally, a point made by many writers is undoubtedly worthy of earnest consideration, that since these catastrophes, whatever may be their immediate cause, invariably have for their ultimate cause delay in the institution of surgical measures, there seems to be no logic or reason for the prolonged medical treatment of cholecystic disease. That advice is not to be taken, of course, as warrant for the performance of cholecystectomy on insufficient indications, particularly on the indication of so-called biliary dyspepsia, or for the performance of operations for the acute disease unless one's convictions happen to take that trend, as the convictions of many still do not. It does seem reasonable, however, not to permit a pathologic process to continue without restraint when its end-results can be as serious as the experiences of every surgeon have proved these to be.

We feel that by this experimental and clinical study we have clearly proved the definite cause and effect relationship between disease of the kidneys and disease of the liver associated with or consequent on disease of the biliary tract, the so-called hepatorenal syndrome. We feel that we have proved that this syndrome occurs not as the result of obstruction but as the result of the release of the obstruction. And we feel that we have proved that the underlying cause of the process is some toxic substance which is water-soluble, which is released by the necrosed cells of the liver and the action of which on the kidneys is not specific but simply a corollary to an overtaxed normal physiologic process, the excretion of foreign proteins by the convoluted tubules. We have evolved the theory, partly from the studies of others and partly from our own clinical and experimental studies, that the so-called hepatorenal syndrome is a pathologic process which may be most marked and most dramatic after operation on the biliary tract but which may occur in several, perhaps many, other diseased states. This theory is that the damaged cells of the liver fail in their function and release thereby some potent toxic substance, which, circulating in the blood, is excreted by the kidneys, but which is so potent that the convoluted tubules, unfitted by nature for such a load, break under it. We believe, further, that in cases in which sudden death occurs with hyperpyrexia, that the hepatic changes, which are the only changes apparent at autopsy, are simply the first stage of the same process which in some cases later terminates in deferred death, with renal as well as hepatic damage.

This report is, as we have mentioned, entirely preliminary. There is still much to be explained. We have as yet no explanation for the hyperpyrexia in the group 1 cases other than the rather vague theory

of an anaphylactic reaction. That the elevation of temperature is in some way related to the liver we are quite sure, our belief being substantiated by the experiments of Andrews, Petersen and Boikan,[33] which establish the fact that in the absence of the liver in eviscerated animals bacterial injections which would ordinarily produce high temperature reactions produce none at all. An endeavor to reproduce these elevations of temperature in animals will be our immediate concern.

We propose, too, to endeavor to isolate the hypothetic toxic substance we have described, and here we shall follow the suggestion of MacDonald and his co-workers[34] that the urine rather than the blood or the tissues is the most potent source of supply for foreign proteins. We shall endeavor to isolate it in such a form that it can be reinjected, with the idea of thus reproducing the hepatorenal lesions we are studying.

We plan, furthermore, to repeat our experiments following hepatic damage with carbon tetrachloride, with prompter injection of the extracts containing the hypothetic toxin. Finally, as clinical material becomes available, we shall repeat our experiments with extracts of the liver of patients dying with hepatic insufficiency, and we shall use these, as well as the extracts of the liver of experimental animals in which obstruction and release of the biliary tree has been done, in stronger concentration. We shall also make more complete observations on the blood chemistry than we have hitherto made.

SUMMARY

The previous literature of so-called "liver death" is briefly reviewed and its various aspects are correlated.

Twenty-three cases of various types of "liver death" following operation on the biliary tract are analyzed. To this number are added 4 cases following operation on the pancreas and 6 cases of traumatic injury to the liver, all of which present the same syndrome.

A series of experiments designed to reproduce the syndrome in experimental animals is reported, and those experiments which were successful are discussed in detail.

The theory is advanced that sudden death, with high temperature, and the so-called hepatorenal syndrome are successive stages of the same pathologic process. The presumptive mechanism of this process is set forth.

The theories of "liver death" hitherto advanced are analyzed.

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33. Andrews, E.; Petersen, W. F., and Boikan, W.: Observations of Eviscerated Dogs, Proc. Soc. Exper. Biol. & Med. **25**:109 (Nov.) 1927.

34. MacDonald, R. F.; Thomas, W. A., and Andrews, E.: Preparation of Blood-Free Tissue Proteins, Proc. Soc. Exper. Biol. & Med. **25**:246 (Jan.) 1928.

The occurrence of the same syndrome in other conditions, such as burns, intestinal obstruction and disease of the thyroid, is noted, and its relation to the latter diseases is discussed.

Further lines of investigation are outlined.

This work has been done with the cooperation and approval of Dr. Urban Maes, director of the Department of Surgery of the Louisiana State University Medical Center. We have been materially aided in the experimental phase of the study by Dr. Ralph Lambert of the Department of Surgery, Dr. Louis Lichtenstein of the Department of Pathology and Dr. W. B. Wright of the intern staff of the Charity Hospital. Miss Genevieve Montz, technician in the Department of Surgery, is responsible for all of the laboratory work.

SEQUELAE OF PEPTIC ULCER FOLLOWING MEDICAL AND SURGICAL TREATMENT

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It has now become generally understood that the treatment of peptic ulcer consists of a thorough medical regimen before an operation is considered. For that reason physicians are now encountering complications from prolonged medical management as well as those which result from improper selection of patients that need to be operated on.

It seems better not to differentiate between gastric and duodenal lesions on the ground of malignant transformation. The etiology is apparently the same for both gastric and duodenal lesions, and the symptoms are essentially the same. Most clinicians that have had the opportunity to observe the clinical course of gastric neoplasm and of gastric ulcer under medical management feel definitely that malignant transformation in gastric ulcer is rare. For that reason one need not be concerned with a different method of treatment of gastric and of duodenal ulcer to prevent malignant changes. Certainly, experience in the clinic for gastric diseases of the Fourth Medical and Surgical Division of the Bellevue Hospital shows that the occurrence of malignant degeneration in gastric ulcer [1] is practically negligible. It is worth while to call attention to the fact that carcinoma of the duodenum [2] is not an uncommon observation but that at present there is no authentic case of malignant degeneration of duodenal ulcer. This helps to support the contention that carcinoma of the stomach is really a rare sequela of gastric ulcer. At the onset carcinoma may resemble an ulcer in gross appearance, but the symptomatology and clinical course are entirely different in carcinoma and in gastric ulcer.

The internist now dictates, in the majority of instances, the time at which a patient with ulcer is referred for operation. As a result a high percentage of patients are carried too long under medical treatment. Certain complications arise which could have been prevented if the

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Clinic held before the Graduate Fortnight of the New York Academy of Medicine on Oct. 22, 1934.

1. Hinton, J. W.: Clinical Consideration of Gastric Ulcer and Carcinoma, Arch. Surg. **27**:395 (Aug.) 1933.

2. Hinton, J. W.: Does Carcinoma of the Duodenum Ever Arise from Duodenal Ulcers? Am. J. M. Sc. **181**:843 (June) 1931.

patient had been referred for operation at an earlier date. One of these complications is chronic pancreatitis, and the second, massive hemorrhage of a recurring nature. These are two complications of ulcer occurring under medical treatment that necessitate surgical intervention. Chronic pancreatitis is really the one true indication for referring a patient suffering from chronic ulcer for operation. One encounters difficulty in making an early diagnosis of such an associated disease, as there are no laboratory aids that are of definite help at this time and one has to rely on the changing symptomatology and on clinical judgment.

The history is the most important aid in the diagnosis of chronic pancreatitis [3] in the advanced stages. The patient usually says that his pain is more severe than at the onset of his complaints and that the dull discomfort which he had when the ulcer was first diagnosed has disappeared. Food gives little relief; he is awake several hours at night because of pain, and he frequently requires sedatives before he can sleep. The pain radiates directly through the lumbar region and is usually felt on both the right and the left side of the spine. Physical examination reveals epigastric tenderness and tenderness over the lumbar region which is usually marked on both sides of the spine; the results of physical examination are otherwise normal. The usual laboratory tests help little in the prognosis [4] of the course of ulcer. My associates and I carried out the amylase test of the blood serum according to the method of Elman and his co-workers [5] and the lipase test of the serum according to the method of Cherry and Crandall,[6] in the hope of detecting cases of early chronic pancreatitis before the symptomatology of ulcer had changed; it was hoped that with infection and fibrosis of the pancreas the amounts of amylase and lipase would be constantly reduced in patients suffering from associated pancreatitis, but the results were extremely variable and of no clinical significance. After employing the tests on forty patients, we discontinued their use. While carrying out experiments on dogs in which we ligated the pancreatic ducts to produce changes in the thyroid gland, we studied the content of amylase and of lipase in the blood of fifteen of the

3. Hinton, J. W.: Chronic Pancreatitis Associated with Peptic Ulcer, Arch. Surg. **28**:580 (March) 1934.

4. Hinton, J. W., and Frankel, Sophie: The Significance of Laboratory Studies in Gastric and Duodenal Ulcers, Am. J. Surg. **17**:25 (July) 1932.

5. Elman, Robert; Arneson, Norman, and Graham, E. A.: Value of Blood Amylase Estimations in the Diagnosis of Pancreatic Disease, Arch. Surg. **19**:943 (Dec.) 1929.

6. Cherry, I. S., and Crandall, L. A.: The Specificity of Pancreatic Lipase: Its Appearance in the Blood After Pancreatic Injury, Am. J. Physiol. **100**:226 (April) 1932.

animals at weekly intervals until they died. The average duration of life was four weeks. Even in the animals in which complete fibrosis of the pancreas developed, the results of the tests were variable and could not be considered of clinical significance.

REPORT OF CASES

Two cases are reported to illustrate the importance of the history in making a diagnosis in these cases.

CASE 1.—A woman, aged 52 years, was seen first on Jan. 17, 1934, complaining of abdominal pain of two and a half years' duration.

The patient stated that in July 1931 she had had a sudden attack of severe pain in the upper part of the abdomen, which necessitated her calling a physician. He gave her an injection of morphine, and the pain was immediately relieved. The next day she felt well. She was then told that her gallbladder was diseased. A few days later roentgenograms were taken of the stomach and gallbladder, which revealed disease of the gallbladder and a normal stomach. The patient then was careful of her diet and had no complaints until three months before consulting me, when she began to have slight discomfort in the upper part of the abdomen but no severe pain. Ten days before her visit to my office she had another attack of severe pain in the upper part of the abdomen, which necessitated her physician's giving her an injection of morphine. She was in bed four days with slight fever, attended by a nurse. Her physician told her that she had a diseased gallbladder and advised operation.

Examination revealed slight epigastric tenderness, but no masses were felt in the abdomen. Moderate tenderness was detected under the right costal arch. The results of urinalysis were negative; the blood count revealed 4,400,000 red cells, 96 per cent hemoglobin (Sahli), 4,100 white cells and 64 per cent polymorphonuclears. Roentgenography failed to visualize the gallbladder after the administration of a dye.

A diagnosis of cholecystitis and cholelithiasis was made, and the patient was operated on at the New York Post-Graduate Medical School and Hospital on Jan. 20, 1934.

Operation.—When the abdomen was opened a normal gallbladder was observed, both on inspection and on palpation. Both kidneys were seen to be normal in size and position. The stomach appeared normal, but on palpation of the common duct it was observed that the pancreas was enlarged and contained a mass as large as an average-sized orange and that the duodenum was adherent to the mass. The diagnosis of perforated ulcer of the posterior portion of the duodenum was made, and a resection of the stomach was then performed, with removal of 75 per cent of the stomach and of 1½ inches (3.81 cm.) of the duodenum. An ulcer the size of a 25 cent piece, which had perforated into the pancreas, was observed in the posterior portion of the duodenum. A pancreatic abscess exuded pus at the time of operation. An anticolic anastomosis was made without enteroenterostomy, and the abdomen was closed in anatomic layers with drainage. The patient made an uneventful convalescence and was discharged from the hospital fifteen days after operation.

The pathologic diagnosis was perforated ulcer of the pyloric region, with pancreatic tissue embedded and attached to the serosal layer of the stomach and duodenum.

This case is cited to illustrate the significance of an accurate history in the diagnosis of chronic pancreatitis associated with duodenal ulcer. On the tenth postoperative day the son-in-law informed me that the patient was a Christian scientist and had never admitted the pain or discomfort which she had suffered between the first attack of pain and that which she complained of three months before consulting me. The patient, according to his statement, had had epigastric distress and vague abdominal pain for a year preceding the acute attack of pain which occurred in July 1931 and persistent discomfort from that time until her operation.

CASE 2.—A man, aged 38, entered the clinic for patients with gastric disease of the Fourth Division of the Bellevue Hospital in March 1930 with a history of severe pain in the upper part of the abdomen and of operation for ulcer. From 1920 to 1925 the patient had had vague symptoms in the upper part of the abdomen, with pain, gas and indigestion. He entered the Jersey City Hospital in March 1925, where roentgenograms were taken of the stomach. A report of pylorospasm was made, and operation was performed. The stomach and duodenum were pronounced normal, but an appendectomy was performed for chronic appendicitis. He improved for a period of about six months, and then symptoms similar to those that he had had prior to operation returned. These symptoms persisted until March 1929, when the patient had severe pain, collapsed on the street and was taken to the Jewish Hospital of Brooklyn, where he was operated on for perforated ulcer of the stomach. At that time the ulcer could not be closed, as it had perforated posteriorly. A gastro-enterostomy was done; drains were inserted, and the patient made an uneventful convalescence. Within four months after this operation he began to have severe pain in the upper part of the abdomen. He was under the care of his own physician for several months, but without improvement.

Course of Illness.—At the time of entering the clinic roentgenograms were taken which revealed a gastrojejunal ulcer in the efferent loop of the jejunum but no retention in the stomach at the end of six hours. The patient was under treatment in the clinic through the year 1930 until January 1931. A reexamination of the stomach and duodenum in November 1930 revealed a gastrojejunal ulcer. The patient had shown some improvement; he discontinued treatment at the clinic, and returned to his private physician, under whose care he remained until August 1932. At that time he returned to this clinic, complaining of severe pain in the abdomen which radiated through to the back and necessitated the taking of morphine and codeine for sleep. Roentgenographic examination on Sept. 10, 1932, revealed a gastrojejunal ulcer. Owing to the severe pain in the back which the patient was suffering, a clinical diagnosis was made of gastrojejunal ulcer perforating into the pancreas and chronic pancreatitis. Operation was performed on Oct. 10, 1932, and a gastrojejunal ulcer perforating into the pancreas was observed; the duodenum was also plastered against the head of the pancreas, and the entire head and body of the pancreas were enlarged and indurated. The gastro-enterostomy was dissociated, and the stomach was closed with no. 1 chromic gut, three layers of sutures being used. The ulcer of the jejunum was so adherent to the pancreas that it necessitated a resection of 5 inches (12.7 cm.) of the jejunum with an end-to-end anastomosis of the jejunum. From palpation and inspection of the duodenum and the pyloric region of the stomach, the ulcer was considered inactive, and owing to the poor condition of the patient it was considered inadvisable to

make a resection at that time. The patient made an uneventful convalescence and left the hospital fourteen days later. He remained under observation in the clinic, and for the first year after his operation he was free from symptoms. In July 1933 he again complained of pain in the abdomen which prevented him from sleeping. He had to take codeine at intervals to obtain sleep. Roentgenograms taken in July 1933 revealed deformity of the duodenum with retention for six hours. The patient was given various medicaments, including Saunders' vaccine, Synadol and gastric mucin, but without improvement. In June 1934 he complained of excruciating pain in his back; he had no abdominal pain and stated that he felt well except for the pain through the lumbar region, which was so severe that his family physician had to administer morphine to obtain relief. The patient was referred by the family physician to the Post-Graduate Medical School and Hospital on June 3, 1934. Examination revealed tenderness in the region over both kidneys and no abdominal tenderness. A diagnosis of chronic pancreatitis resulting from the preexisting duodenal ulcer was made. The pain in his back was so severe that roentgenograms were taken of the genito-urinary tract on June 4 to rule out the possibility of stone. A series of roentgenograms of the gastro-intestinal tract was taken, and a diagnosis of pyloric obstruction due to duodenal ulcer was made. Operation was performed on June 9 with a preoperative diagnosis of ulcer of the posterior part of the duodenum and chronic pancreatitis. After the abdomen was opened the duodenum was seen to be adherent to the head of the pancreas, the head of the pancreas being the size of an orange. A gastric resection was made with the removal of 75 per cent of the stomach and of 1½ inches (3.81 cm.) of the duodenum. An ulcer of the posterior part of the duodenum the size of a 25 cent piece had perforated the entire wall of the duodenum, the base of the ulcer being formed by the head of the pancreas. There was an erosion at the head of the pancreas the length of the distal phalanx of one's little finger and from about 3 to 5 mm. deep. The patient died three days later of peritonitis.

Autopsy revealed peritonitis which had originated in the lesser peritoneal sac, an enlarged pancreas and chronic pancreatitis. The pathologist, Dr. Rabson, considered the chronic pancreatitis as the etiologic factor in the production of the peritonitis of which the patient died.

I wish to call attention to the fact that the patient's pain and symptoms were all referable to the back and that the pain was so severe that it necessitated the use of morphine. The family physician considered that the patient at the time of his admission to the hospital was suffering from a stone in the kidney and that his symptoms were not due to the preexisting ulcer. The interns at the hospital thought that the patient was probably an addict to drugs, as it was necessary to give him morphine for the relief of pain. The observations at operation and at autopsy clearly indicated that the only existing pathologic condition was the perforated duodenal ulcer with chronic pancreatitis.

The management of a bleeding peptic ulcer is one of the most difficult complications which one encounters. The cases of the patients with gross hemorrhage treated medically and surgically in the Fourth Surgical Division were reviewed. These cases were reported,[7] and a

7. Hinton, J. W.: Massive Hemorrhage in Peptic Ulcer: Report of Eighty-Seven Cases, Ann. Surg. **101**:856 (March) 1935.

special grouping of eighty-seven cases of gross hemorrhage was made. It seems worth while to give the classification of cases of hemorrhage as I grouped them on the basis of my study.

Group 1 comprised sixteen cases of hemorrhage occurring in patients with peptic ulcer under competent medical management; group 2, eleven cases of hemorrhage in which operation for acute perforation or chronic ulcer had been performed and in which the catastrophe of hemorrhage had not occurred until months or years after operation; group 3, five cases of hemorrhage occurring in ulcers that had previously been operated on for hemorrhage, in which the patient continued to have recurring hemorrhage after operation; group 4, seventeen cases of severe hemorrhage which occurred in patients with normal histories or with short histories of gastric symptoms, who did not know they had ulcer until the hemorrhage occurred, and group 5, thirty-eight cases in which the patients were admitted with hemorrhage and a long history of symptomatology of ulcer, but without regulated medical management.

From this classification of cases of gross hemorrhage it can be seen that prolonged medical management of a patient who has had one severe hemorrhage after being under adequate medical management is merely inviting another such catastrophe, and for that reason one does not consider prolonged medical treatment for this group of patients.

Case 3.—A man, aged 38, seen at his home on Jan. 11, 1931, gave a history of having been treated for ulcer of the duodenum for the two and a half years before I saw him. Two days before consultation with me he had had a slight cold and some abdominal discomfort. He had been practically free from symptoms for one year prior to that time. The night before I saw him he passed dark blood by rectum, and on the morning of my visit he had vomited a large quantity of blood. He was immediately transferred to the Post-Graduate Hospital and given a transfusion of 600 cc. of blood. On January 16 he was operated on, and an ulcer was noted in the first portion of the duodenum. Excision of the ulcer and posterior gastro-enterostomy were then performed, with no. 1 chromic gut used for sutures. The gallbladder was normal, but an appendectomy was performed for chronic appendicitis; the abdomen was closed in anatomic layers. The patient made an uneventful convalescence. The pathologic diagnosis was chronic appendicitis and duodenal ulcer with a tendency to heal. The patient left the hospital twenty-two days after the operation.

This patient has been under constant observation since his operation in January 1931; he has been well since that time and has had no abdominal pain or hemorrhage. I wish to call attention to the fact that the patient had been under a strict and regulated medical regimen and had been free from symptoms for one year prior to the sudden, severe hemorrhage which necessitated hospitalization and operation.

Complications following operation for peptic ulcer include hemorrhage, acute perforation of a peptic or gastrojejunal ulcer, chronic gastrojejunal ulcer and gastrojejunal fistula resulting from the formation of gastrojejunal ulcer.

In considering gross hemorrhage that follows operation for peptic ulcer it is best to consider the classification of hemorrhage given in this paper. This sequela is serious, and the management of each case has to be decided from its course. As a rule reoperations on the patients that have had hemorrhage after the first operation give poor results.

The following case is cited because, on the basis of my classification, the original operation should not have been done.

CASE 4.—A man, aged 38, was seen on Sept. 15, 1934, complaining of slight pain in the epigastrium for four days prior to his admission and of having had hemorrhages from the stomach during the last three and a half years.

The patient stated that in February 1931 he had had a severe gastric hemorrhage, for which he was treated in the Misericordia Hospital of Philadelphia for seven weeks. He was given a transfusion at that time and was later operated on for a duodenal ulcer. At that time a plastic operation was performed on the duodenum, and the patient made an uneventful convalescence, except that a small hernia developed in the upper part of the incision. About one year later (the exact date he did not recall but thought it was about March or April 1932) he had another hemorrhage from the stomach; neither at this time nor during the first hemorrhage did he vomit blood, passing it all by bowel. He had no pain during the time between the operation and the second hemorrhage; he had had no symptoms referable to the stomach preceding the first hemorrhage, but he suddenly collapsed as the result of the hemorrhage. He was treated medically at this time. Approximately one year after this hemorrhage, in the spring of 1933, he had another hemorrhage; it was also from the bowel. He was again treated medically and was well until February 1934, when he again had a hemorrhage from the stomach. He had had no pain or abdominal discomfort until approximately ten days before consulting me, and the slight abdominal pain became a little more severe four days before the visit. At the time of my examination he had a definite ventral hernia and slight epigastric tenderness. The blood count showed 4,600,000 red cells, 87 per cent hemoglobin, 9,000 leukocytes and 67 per cent polymorphonuclears. He was given a Sippy diet as planned for the third week and an injection of Saunders' vaccine, and was advised to return two days later for roentgenography. On the same night after he consulted me he had a slight hemorrhage with a dark stool. He was referred immediately for roentgen examination, which revealed an ulcer of the posterior part of the duodenum. Dr. Spillman reported that because of a persistent notch on the inferior surface of the cap, which is characteristic of duodenal ulcer, he thought the patient should be operated on, as the lesion was uncomfortably close to the superior pancreaticoduodenal artery.

This patient undoubtedly had two ulcers at the time of his first operation, one on the anterior and one on the posterior portion of the duodenum. The plastic operation eradicated the ulcer on the anterior surface, but that on the posterior surface remained. In view of the recurring hemorrhages and the location of the ulcer, the patient was

advised to have a second operation, as it was feared that he might have a sudden fatal hemorrhage. Of course, it would be necessary to make a subtotal resection in this case.

The occurrence of perforated ulcers of the stomach and duodenum apparently is on the increase,[8] and the accepted method of management in most clinics is simple closure and the reservation of more radical procedures until a later date. Therefore, it is natural to expect that in a reasonable number of these patients reperforation will occur, as is occasionally seen.

CASE 5.—A man, aged 37, was first seen in February 1927, complaining of abdominal pain occurring after meals and occasionally at about 2 or 3 a. m. for from six to nine months. The patient stated that for about eight or nine months before consulting me his symptoms had grown gradually worse. The physical examination revealed epigastric tenderness; otherwise abdominal examination revealed nothing abnormal. A diagnosis of duodenal ulcer was made. Roentgenograms taken at the Post-Graduate Hospital on Feb. 18, 1927, revealed a duodenal ulcer without six hour retention. The patient did well under medical treatment until Jan. 18, 1929, when he was seized with severe abdominal pain. A diagnosis of perforated duodenal ulcer was made, and he was operated on at the New York Post-Graduate Medical School and Hospital. Perforation of a duodenal ulcer was noted, and a Horsley pyloroplasty and appendectomy were done. The patient made an uneventful convalescence and was discharged on the fifteenth postoperative day. He was free from symptoms until Sept. 29, 1929, when he was awakened at about 2 a. m. with severe abdominal pain and was taken immediately to the Post-Graduate Hospital with a diagnosis of perforated duodenal ulcer. He was operated on, and a perforation of a duodenal ulcer was observed. Excision of the ulcer was made, and the duodenum was closed with no. 1 chromic gut. Cholecystectomy was also done, and the abdomen was closed in anatomic layers. The patient made an uneventful convalescence and was discharged from the hospital on the sixteenth postoperative day. He remained well and free from symptoms until November 1931, when he began to have epigastric distress, which persisted for about six weeks. On Dec. 2, 1931, he consulted me at my office. The physical examination revealed nothing abnormal, although he complained of slight epigastric distress. Immediately on leaving my office and returning to his residence, he had severe abdominal pain and was taken immediately to the Post-Graduate Hospital, where he was operated on for a third perforated duodenal ulcer. Excision of the ulcer was made, and the abdomen was closed in anatomic layers. The patient again made an uneventful convalescence and was discharged from the hospital on the seventeenth postoperative day. After this operation he was free from symptoms for six months, but from September 1932 he had slight epigastric pain and was under constant medical treatment. On Dec. 30, 1932, he was awakened by a feeling of nausea and had a severe gastric hemorrhage. He was again admitted to the New York Post-Graduate Medical School and Hospital and received a transfusion of 750 cc. of blood on three occasions. He remained in the hospital three weeks. After this hemorrhage he continued to have slight epigastric distress and was never entirely free from symptoms through the year 1933, although he

8. Hinton, J. W.: Incidence of Peptic Ulcer and Its Complications, Am. J. Surg. **20**:102 (April) 1933.

remained on a strict Sippy regimen, did not use alcohol or tobacco and was careful of his hours. In January 1934 he was having severe pain. Roentgenograms taken at that time revealed a duodenal ulcer, and he entered St. Luke's Hospital on Feb. 13, 1934, where he was operated on for duodenal ulcer. Operation revealed a duodenal ulcer on the superior portion of the duodenum; subtotal resection was performed with the removal of 75 per cent of the stomach, and an anticolic anastomosis without entero-enterostomy was made. The patient made an uneventful convalescence during the first three days; the abdomen then became distended, and he was critically ill for five days. He seemed to improve and to be out of danger, but he died suddenly on the twelfth postoperative day. Autopsy revealed complete necrosis of the pancreas and hemorrhage from the pancreatoduodenal artery.

This case is cited to illustrate the tendency of ulcer to recur although the ulcer has been completely excised in previous operations.

Acute perforation of a gastrojejunal ulcer is seen in cases in which a diagnosis of ulcer has never been suspected, and the following case illustrates a late marginal ulcer.

CASE 6.—A man, aged 41, was admitted to the Bellevue Hospital on Nov. 15, 1933, with a history of severe epigastric pain of a few hours' duration. The patient gave a history of having been operated on at the Governeur Hospital in October 1920 for ulcer of the stomach. The records from that institution revealed that he had had a posterior gastro-enterostomy for pyloric ulcer on Oct. 2, 1920, and that he had given a history of epigastric pain for two years preceding the operation. After the operation he had had slight attacks of epigastric distress, but, generally speaking, he had been in good health and considered himself cured of the ulcer. At the time of his admission he was suffering from severe abdominal pain of a few hours' duration. Examination revealed marked rigidity and tenderness of the abdomen, and a diagnosis of perforated ulcer was made. A laparotomy revealed a perforated gastrojejunal ulcer, the perforation being on the stoma. A simple closure of the perforation was made, and the patient made an uneventful convalescence and was discharged from the hospital on the nineteenth day. This patient has been in the clinic of the Fourth Division of the hospital since his discharge. He has been essentially free from symptoms, and roentgenograms taken on Aug. 6, 1934, revealed a gastro-enterostomy opening which functioned normally. However, slight tenderness over the stoma and defective filling at the base of the duodenum with a retention of six hours, characteristic of duodenal ulcer, were noted.

Chronic gastrojejunal ulcer does occur after both gastro-enterostomy and subtotal resection. The incidence after gastro-enterostomy is much higher than is admitted in most clinics, provided one is careful to observe these patients over a period of years. On the basis of observation in this clinic, the frequency of 2 or 3 per cent for marginal ulcer after gastro-enterostomy, as reported from most clinics, in no way expresses the true incidence of this sequela. According to the observations of my associates and me, gastrojejunal ulcer occurred in 16.4 per cent of eighty-five patients with gastro-enterostomy [9] who have been

9. Church, Reynold, and Hinton, J. W.: A Study of Six Hundred and Seventy-One Cases of Peptic Ulcer with Special Emphasis on One Hundred and Fourteen Post Operated Cases, New York State J. Med., to be published.

under observation in this clinic during the past five years. It is worth while to remember that the longer the patients are under observation, the higher the incidence of gastrojejunal ulcer will be.

Gastrojejunal-colic fistula is not unusual; it results from the formation of a gastrojejunal ulcer on the anterior line of the anastomosis of the stoma, the ulcer actually being located on the jejunum. The transverse colon becomes adherent to the ulcerated area, and the ulcer gradually erodes and perforates the entire wall of the jejunum and later that of the transverse colon. At first the opening is relatively small, but as the condition progresses the opening becomes larger, and the patient suffers from extreme diarrhea and emaciation, associated with abdominal pain on the left side.

In the following case a spontaneous gastrocolic fistula developed while the patient was under medical treatment.

CASE 7.—A woman, aged 60, was first seen at the clinic on Dec. 4, 1930, with a history of epigastric pain and indigestion for a period of ten years.

The patient stated that for a period of ten years she had had slight epigastric distress and gas; for eight months prior to her admission she had had severe pain, and for the last six months she had been vomiting several times a week. Roentgenograms taken Oct. 30, 1930, before admission to the clinic, revealed an ulcer of the lesser curvature in the pars media, with retention for six hours of two thirds of the motor meal. The diagnosis was that of gastric ulcer.

The physical examination revealed a rather poorly nourished woman weighing 111 pounds (50.3 Kg.). The Wassermann test gave a 4 plus reaction. It was believed probable that the patient had a syphilitic ulcer of the stomach. An operation was advised, but she refused to permit it; therefore she was put on an ambulatory medical regimen, as her husband was paralyzed and she refused to enter the hospital for rest in bed. The patient was fairly conscientious and remained under the care of physicians at the clinic until Jan. 26, 1933. During her period of treatment her weight remained the same, between 110 and 115 pounds (49.9 and 52.1 Kg.). A follow-up visit to the home on June 8, 1933, failed to reveal the patient at the address which had been given. No information could be ascertained as to her whereabouts. The patient had numerous roentgen examinations while under care at the clinic, all of which revealed the same condition as had the first examination. She was examined on March 2 and June 15, 1931; on Jan. 7, May 4 and Oct. 16, 1932, and on Jan. 30, 1933, on all of which occasions a gastric lesion was revealed with a six hour retention of from one half to three fourths of the motor meal. During the period under which she was under treatment at the clinic, she was receiving antisyphilitic treatment in the dermatologic department of the Bellevue Hospital; the Wassermann reaction remained positive while she was under antisyphilitic treatment. The patient was brought into the hospital on July 16, 1934, as presenting an emergency case, and was admitted to the Fourth Medical Division. At that time she gave a history of diarrhea for two or three months and stated also that she had had diarrhea for four years. I wish to call attention to the incorrectness of this statement, for she never complained of diarrhea during the three years that she was under constant treatment in the clinic. The diarrhea was of moderate severity with from two to four movements of the bowels

a day. Roentgen examination and a series of roentgenograms of the gastro-intestinal tract made on July 21, 1934, revealed a gastrocolic fistula. Figure 1 shows the entire meal lying in the colon immediately after the barium was administered. This picture should be contrasted with figure 2, taken at the time of the patient's admission to the clinic in October 1930, which reveals a large gastric ulcer and

Fig. 1.—Roentgenogram taken July 21, 1934, immediately after administration of the barium meal which lies entirely in the colon.

marked retention of the motor meal. The patient was in a critical condition; she refused to undergo operation and died on Aug. 3, 1934. Autopsy revealed a gastrocolic fistula, which is illustrated in figure 3. The fistula was spontaneous and, in all probability, syphilitic, although spirochetes were not demonstrated and no other evidence of syphilis was seen at the time of autopsy.

This case illustrates an unusual complication of gastric ulcer occurring while the patient was under medical care. The patient had been advised to undergo operation, but she refused to consider surgical intervention.

Fig. 2.—Roentgenograms taken in October 1930, showing gastric ulcer of the lesser curvature and retention of two thirds of the motor meal in the stomach.

As physicians are interested in the prevention of complications which may occur in patients suffering from peptic ulcer, they are forced to revise some of the accepted indications for operation. The internist in the past and at present usually accepts two conditions as true indications for operation—first, a gastric lesion, because of his fear of malig-

nant degeneration, and, second, gastric retention of from 50 to 75 per cent of the meal at the end of six hours. Unfortunately, these two conditions are not true indications for surgical treatment, and in the majority of instances gastric lesions respond to medical management much more readily than duodenal lesions. Also in 75 or 80 per cent of the patients suffering from gastric retention of 50 or 75 per cent of the meal at the end of six hours, the stomach will completely empty under proper medical management. On the other hand, pain which is persistent without periodicity is a true indication for referring patients for surgical treatment. It is a patient of this type that the internist

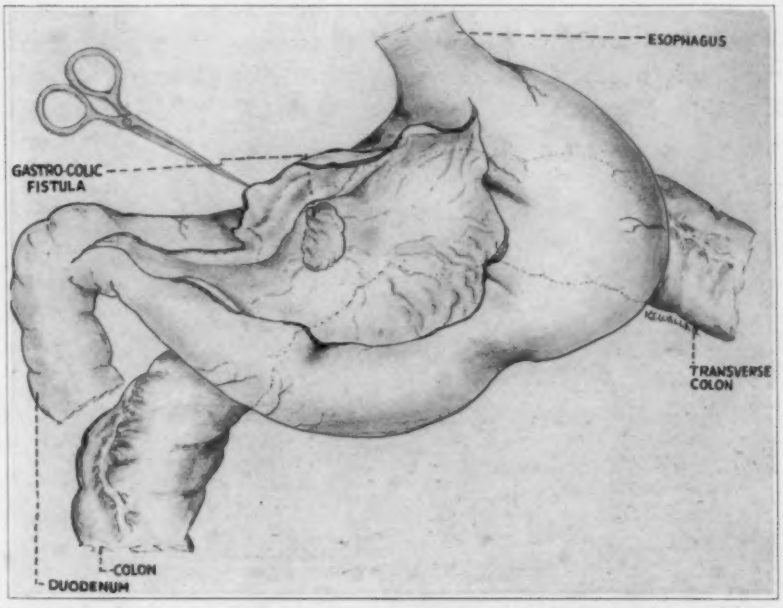

Fig. 3.—Drawing showing the position of the gastrocolic fistula.

frequently hesitates to submit to surgical treatment, believing that, since the stomach empties normally and there is no pyloric obstruction, the patient will ultimately respond to medical management. This is not true, and a patient of this type, as has been stated before, is suffering from an associated lesion, which is usually chronic pancreatitis. When the pancreas becomes involved in an associated infection the medical management should be immediately discontinued and the patient referred for operation.

A discussion of the incidence of gastrojejunal ulcer elicits considerable comment and difference of opinion from physicians in all the large clinics in the country. It can only be stated that, on the basis of

observations in this clinic, it is believed that the incidence of 16.4 per cent in cases of gastrojejunal ulcer after gastro-enterostomy is an underestimation, rather than an overestimation, of the exact frequency of occurrence of this complication. A large number of patients are returning with gastrojejunal lesions as well as with gross hemorrhage as the clinic grows older.

There is no condition in medicine at present in which clinical judgment plays such an important part in the selection of the method of treatment for the patient as it does in peptic ulcer. Whether the treatment should be medical or surgical is a decision that is based to a great extent on clinical experience. Many of the mistakes that are made and the poor results that are obtained from medical and surgical management are due to the physician's relying too closely on the laboratory findings of hyperacidity and on the report, based on roentgenologic findings, of normal evacuation of the stomach at the end of six hours.

130 East Seventy-Ninth Street.

FIFTY-SEVENTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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CONGENITAL DEFORMITIES

Congenital Dislocation of the Hip.—In a detailed statistical study of 387 cases of congenital dislocation of the hip, representing 501 dislocated hips treated during the period of 1915 to 1933, Steindler and his co-workers [1] reported the results of both closed and open methods of reduction. They concluded that the results of the closed method were not as conclusively satisfactory as those reported by other authors and that the results became definitely worse with duration of the period of observation. They expressed the belief that in order to be accurate, the end-results should be regarded as significant only after full growth has been obtained. The authors used open reduction as a supplementary method and therefore did not attempt to compare the results obtained by open with those obtained by closed reduction. They considered the indications for open reduction to be the inability to reduce or to maintain reduction by closed methods. The upper age limit for open reduction they considered to be 11 years. The authors have included an excellent statistical study which is too detailed for inclusion

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This report of progress is based on a review of 136 articles selected from 202 titles appearing in medical publications approximately between Nov. 3, 1934, and Feb. 22, 1935. Only those which seemed to represent progress were chosen for review.

1. Steindler, A.; Kulowski, J., and Freund, E.: Congenital Dislocation of the Hip: Statistical Analysis, J. A. M. A. **104**:302 (Jan. 26) 1935.

in this summary but should be read by all who are interested in the treatment of congenital dislocation of the hip.

POLIOMYELITIS

Convalescent Serum in the Treatment of Poliomyelitis in the Preparalytic Stage.—Fischer [2] studied 447 cases of poliomyelitis in which treatment with serum from convalescent patients was used and 102 control cases occurring in New York City in 1931. The condition three weeks after onset was compared with the end-result six months later, the data being given in tables. Fischer expressed the belief that the value of convalescent serum in the treatment of poliomyelitis in the preparalytic stage was not definitely proved because, in spite of every effort to obtain comparable data, it was not possible to do so. The data presented demonstrated that the outcome for the patients given convalescent serum was no better than, if as good, as that for the untreated ones. While in the control patients the attack of poliomyelitis was probably somewhat milder, it appeared that no advantage was shown by the other groups. There was no proof that a physician was depriving his patient of an equal chance for complete recovery by not administering convalescent serum.

A Study of 410 Patients at the Philadelphia Hospital for Contagious Diseases During the Summer and Fall of 1932.—Four hundred and ten patients with conditions suspected of being poliomyelitis were admitted to the Philadelphia Hospital for Contagious Diseases in 1932. In 304 cases (74.1 per cent) the diagnosis was verified. Two hundred and fifty-four patients (68.5 per cent) received serum; 124 of these showed weakness or paralysis on admission, but at the time of discharge the number of patients showing such symptoms had increased to 154. Fifty patients (16.5 per cent) received no serum on admission; of these 28 on admission and 38 at discharge showed weakness or paralysis. Lucchesi [3] concluded that convalescent serum had little or no value in the prevention of paralysis.

A Successful Method for Vaccination Against Acute Anterior Poliomyelitis.—Kolmer and his associates [4] succeeded in preparing from the spinal cords of monkeys an attenuated virus of anterior poliomyelitis; from this a vaccine was obtained and used on 25 children. In 21 of

2. Fischer, A. E.: Human Convalescent Serum in Treatment of Preparalytic Poliomyelitis; Comparison of 447 Treated and 102 Control Patients in New York City in 1931, Am. J. Dis. Child. **48**:481 (Sept.) 1934.

3. Lucchesi, P. F.: Am. J. M. Sc. **188**:515, 1934.

4. Kolmer, J. A.; Klugh, G. F., Jr., and Rue, Anna M.: Successful Method for Vaccination Against Acute Anterior Poliomyelitis, J. A. M. A. **104**:546 (Feb. 9) 1935.

the 25 patients increase in the antibody content of the blood was shown by titration after the inoculations. The authors considered the vaccine as entirely safe for use and expressed the belief that the amount of the antibodies formed is comparable to that found in the blood of naturally immune subjects. The duration of the immunity was unknown, but it had been found to last for two days in monkeys. Kolmer and his co-workers considered that their vaccine was now ready for use in clinics as a protective agent and should be used particularly during the time of epidemics.

[ED. NOTE.—The results of this work seem to be really noteworthy and certainly should be given a thoroughly controlled trial at the earliest opportunity.]

TUBERCULOSIS

Tuberculosis of the Spine in Children.—From a study of 89 children suffering from tuberculosis of the spine Cave [5] concluded that probably the most important factor in determining the degree of deformity was the amount of destruction which occurred in the posterior supporting structures (pedicles and laminae). He stated that rapid progression of deformation may be prognosticated by finding mobile spinous processes in the involved area. From the classification of Doub and Badgley, most rapid destruction was observed in the intervertebral type and the most marked deformity was found in the central type. In this series there were five double lesions, all of which occurred in the lower dorsal and lumbar regions. An abscess containing calcium was almost a certain sign of tuberculosis. Biopsy, culture and inoculation of guinea-pigs were the methods used in making a diagnosis. In 70 of the 89 cases roentgenograms showed an abscess. Treatment in the acute cases consisted in recumbency on a Bradford frame with gradual hyperextension and, later, application of a plaster jacket. The average period of recumbency was thirty-three months for the patients who had not undergone operation; for those who were operated on it was thirty-nine months. Operative fusion of the spine was carried out when deformity increased in spite of hyperextension. Cave stated that every attempt should be made to prevent deformity and that fusion may insure healing without apposition of adjacent vertebral bodies. The end-results in the 89 cases were classified as follows: excellent, 18; good, 26; fair, 10; poor, 10. Twenty of the patients died, and in 5 cases the nature of the end-results was unknown.

Tuberculous Tenosynovitis of the Hand.—In a carefully prepared monographic article on tuberculous tenosynovitis of the hand Mason [6] outlined the symptoms, clinical course and pathologic changes in, and

5. Cave, E. F.: New England J. Med. **211**:578, 1934.
6. Mason, M. L.: Surg., Gynec. & Obst. **59**:363, 1934.

prognosis of, the disease. He concluded that the best treatment was the surgical excision of the diseased tissue, including the visceral layer of the tendon sheath. In some instances diseased portions of the tendons themselves had to be sacrificed. The optimum location for incision, the operative technic and the after-care were described in detail.

OSTEOMYELITIS

The Stewart Treatment for Osteomyelitis.—Kline [7] reviewed 5 cases, 4 of chronic osteomyelitis lasting for periods varying from six months to eighteen years and 1 of a severely infected wound. Healing was complete in every case in from thirty to seventy-five days. The Stewart [8] method of treatment called for a 0.25 per cent solution of trinitrophenol prepared with distilled water to which glycerin was added to the amount of 8 per cent. The solution was sprayed into small wounds, poured into large ones and forced through fistulous tracts with a soft rubber catheter and a 5 cc. Luer syringe. Immediately after application of the trinitrophenol solution an autoclaved suspension consisting of 20 Gm. of calcium carbonate and 215 cc. of distilled water was applied to the wound. Kline found that granulation tissue formed promptly, purulent exudate was reduced, healing was rapid, pain and discomfort were minimized and the residual scar was less marked.

Acute Osteomyelitis.—Fraser [9] regarded acute staphylococcic osteomyelitis as a local manifestation of a general local reaction, calling into being strong antibacterial influences, which were efficient in counteracting the general sepsis. He advocated a modified form of Starr's operation. It was suggested that the localization of infection in the metaphyses of long bones may be due to the fact that these areas are rich in reticulo-endothelial tissue, which is one of the most important defensive mechanisms of the body against general infection.

Nature and Treatment of Acute Osteomyelitis.—Conservative methods in the treatment of acute osteomyelitis were advocated by Holman,[10] who considered that this condition was merely a local manifestation of systemic infection. Expectant treatment and immobilization were used until there was definite evidence of the formation of pus. In the majority of cases simple incision of the periosteum was all that was necessary at the primary operation. While sequestrums were frequently formed and had to be removed at a second operation, in some cases they were absorbed. Only one death occurred in a group of 29 patients treated by the conservative method.

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7. Kline, L. B.: Mil. Surgeon **75**:251, 1934.
8. Stewart, M. N.: Surg., Gynec. & Obst. **58**:155, 1934.
9. Fraser, J.: Brit. M. J. **2**:539, 1934.
10. Holman, C. C.: Lancet **2**:867, 1934.

[ED. NOTE.—There is a growing conviction that in cases of osteomyelitis and other infections the patient should not be forgotten in attempts to treat local manifestations of a systemic disease. The resistance of the patient and the reparative forces of the body should be helped and not retarded by the therapeutic measures used.]

CHRONIC ARTHROPATHIES

Some Metabolic and Nutritional Aspects of Chronic Arthritis.—Pemberton [11] in a general paper stressed the importance of a balanced diet, particularly for relief of edema about the joints. He stated that edema disappeared with a diet with a low carbohydrate and a high protein content. Three and six-tenths grams of water was retained in the body for every gram of carbohydrate stored. A diet with a high protein content required available water for the elimination of protein metabolites. A diminution of pain was usually found to accompany a negative water balance. In the majority of advanced cases of chronic arthritis dysfunctions of the gastro-intestinal tract were present. Pemberton stated that chronic arthritis is a generalized disease with certain "prodromes." Coordination of various lines of therapy based on sound physiologic premises should control the disease in 80 per cent of the cases.

Rheumatoid Arthritis and Its Treatment with Gold Salts.—Forrestier [12] reported that from 70 to 80 per cent of patients with rheumatoid arthritis had responded well to therapy with gold salts. He observed a series of 500 cases. The best results were obtained when treatment was given in the early stages, but in 12 cases of chronic arthritis with irreducible ankylosis of one or many joints, reduction under anesthesia was made possible, without any subsequent inflammatory reactions, when a preliminary course of injections of gold salts was administered. Forrestier advanced the hypothesis that the development of rheumatoid arthritis is accompanied by tuberculous infections but that it requires another infective element, such as tonsils or teeth, to provide it.

[ED. NOTE.—One of the editors is familiar with the work reported by Forrestier. Many other measures, both medical and orthopedic, are used by him in the treatment of this condition. The use of heavy metals in colloidal suspension probably has a definite but limited application in the treatment of chronic arthritis, particularly in patients past middle life, in whom stimulation of the reticulo-endothelial system seems at times to be indicated.]

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11. Pemberton, R.: Am. J. Digest. Dis. & Nutrition **1**:438, 1934.
12. Forrestier, J.: Lancet **2**:646, 1934.

Neuropathic Disease of the Joints.—Bergmann [13] expressed the opinion that the pathologic alterations in neuro-arthropathies are understandable on the basis only of trophic disturbances. He expressed the belief that mechanical influences play only a small rôle in the development of the lesion and that antisyphilitic treatment is of some value in treatment in the early stages of the disease. Early diagnosis is difficult. He stated that he had no experience with operative fusion of the knee but that on the basis of Oehlecker's and Payr's experiences he was inclined to advise against such procedures.

[ED. NOTE.—Early operative fusion of the knee in tabetic patients has been found to be a satisfactory procedure in the experience of one of the editors. The histopathologic changes in the joints in patients with neuropathic diseases as outlined by Moritz suggest that trauma plays a considerable rôle in the development of the disorder in the joints.]

THE SPINE

Treatment of Kyphosis in Adolescent Patients.—Calvé [14] stated that the spontaneous natural curves formed to compensate for kyphosis in adolescent patients are unsatisfactory because pain follows in the lumbar area of hyperextension. Therapeutic compensation consists in bringing about extension curves immediately above and below the area of kyphosis. The method that he advocated to secure therapeutic compensation was recumbency in a position of hyperextension on a shaped plaster bed. He stated that this method is better than the wearing of plaster jackets, for it permits the application of physical therapy to the muscles of the trunk, on the strength of which the maintenance of the new position depends.

[ED. NOTE.—The development of compensatory curves in kyphosis in adolescent patients, frequently called epiphysitis of the spine in America, is not always necessary. The procedures used to correct the kyphosis in patients with tuberculosis or chronic arthritis of the spine are frequently effective in the treatment of kyphosis in adolescent patients.]

PERIPHERAL VASCULAR DISTURBANCES

Passive Vascular Exercises.—The treatment of obliterative arterial diseases by a new "Pavaex" apparatus was described by Herrmann and Reid.[15] The limb was encased in a machine applying rhythmic alterations of pressure similar to those applied by the respirator used in the

13. Bergmann, E.: Deutsche Ztschr. f. Chir. **243**:761, 1934.

14. Calvé, J.: Brit. M. J. **2**:983, 1934.

15. Herrmann, L. G., and Reid, M. R.: Passive Vascular Exercises; Treatment of Peripheral Obliterative Arterial Diseases by Rhythmic Alteration of Environmental Pressure, Arch. Surg. **29**:697 (Nov.) 1934.

treatment of infantile paralysis. The authors reported that they had used the machine in 51 cases of organic obliterative arterial disease, and they expressed the belief that the device hastened the establishment of collateral circulation to a more normal state, as evidenced by increase in the temperature of the skin. In 86 per cent of their cases improvement was noted; in 14 per cent, no improvement occurred.

The Digital Vascular System.—Popoff [16] gave a well illustrated review of the digital vascular system in normal and in pathologic states. He described the specialized arteriovenous anastomosis (glomus) which regulates the local temperature and flow of blood and assists in regulating the temperature of the body. He stated that the improper development or the absence of this glomic system is probably the cause of many thermic and trophic disturbances. No glomus is found in supernumerary digits. These anastomotic units atrophy in old age. In cases of arteriosclerotic gangrene changes in the glomus are due primarily to hyaline degeneration in the afferent artery of the glomus. In cases of diabetic gangrene the intima of the Sucquet-Hoyer canal and that of the preglomic arterioles are the first to show primary degenerative changes. In cases of thrombo-angiitis obliterans the glomic system appears to be free from primary specific changes. The trophic changes in thrombo-angiitis obliterans were attributed by the author to abnormal anastomoses between arteries and veins. Two types of abnormal anastomoses were observed: a lateral type and a terminal type. Popoff stated that consideration of the glomic system is important in interpreting the symptoms and findings in circulatory disturbances occurring in the hand.

NEOPLASMS

Tumors of the Tendon Sheaths, Joints and Bursae.—After reviewing the embryologic development of articular structures Geschickter and Lewis [17] classified neoplasms arising from these structures. The common neoplasms of the tendon sheaths were benign osteochondromas and ganglion and giant cell tumors, all of which showed a relationship to hemangioma and lymphangioma. Tumors of the tendon proper and sarcoma were rare. Chondrosarcoma at or near the insertion of tendon into bone and fibrosarcoma of the tendon sheath were described. The most frequent neoplasms of joints were benign osteochondromas or chondromas involving the synovial membrane diffusely (osteochondromatosis) and giving rise to multiple loose bodies. The authors stated that cysts and cartilaginous free bodies of questionable neoplastic nature

16. Popoff, W.: Digital Vascular System, with Reference to State of Glomus in Inflammation, Arteriosclerotic Gangrene, Diabetic Gangrene, Thrombo-Angiitis Obliterans and Supernumerary Digits in Man, Arch. Path. **18**:295 (Sept.) 1934.

17. Geschickter, C. F., and Lewis, D.: Am. J. Cancer **22**:96, 1934.

may arise from the articular cartilages. Xanthomatous giant cell tumors occurred in the synovial membrane, occasionally invading the articular cartilage and invading bone. They apparently arose in mesenchymal condensations at the primordium of the sesamoid bones and resembled similar tumors within the tendon sheaths. Fibromas, fibrosarcomas and lipomas were described. Bursal tumors were said to be rare. Only 30 cases could be collected from the literature and the records of the Johns Hopkins Hospital laboratory. Benign and malignant chondromatous lesions and spindle cell sarcoma predominated. The prepatellar bursae were most often affected.

Biologic Relationship of Tumors of the Tendon Sheath to Tumors of the Joints and Bursae.—Morton[18] in a review of the histologic characteristics of these lesions called attention to the fact that these various tumors of the tendon sheaths are closely related to the tumors of joints and bursae and that the basic cell of all these tumors is the synovial cell, which is a modified mesenchymal cell with the ability to revert in the direction of the fibroblast or to produce cartilage and bone. He therefore gave the following classifications of benign tumors of the tendon sheaths, bursae, joint capsules and joint linings:

Tumors of the Tendon Sheaths	Tumors of the Joints and Bursae
Synovioblastoma "ganglion"	Synovioblastoma
Fibroma	Fibroma
Chondroma or osteochondroma	Intra-articular, Extra-articular chondromatosis
Giant cell xanthoma	Giant cell synovial membrane tumors
Angioma	Angioma
Hemangioma	Hemangioma
Lymphangioma	Lymphangioma
Lipoma	Lipoma

In the group of malignant tumors Morton placed the synoviogenic sarcomas. These contain many of the elements derived from the synovial membranes or from the tissues in apposition to them. The cases reported are as yet too few to permit classification of the tumors into anatomic types. Metastatic involvement of tendons, bursae or joints practically never occurred.

Bony Metastases from Malignant Conditions of the Prostate.—The following types of bony metastases from primary carcinoma of the prostate were presented by Olin:[19]

1. Osteoplastic: In cases of osteoplastic metastases the roentgenogram showed areas of bone much more dense than the surrounding

18. Morton, J. J.: Surg., Gynec. & Obst. **59**:441, 1934.
19. Olin, H.: Illinois M. J. **66**:388, 1934.

normal bone. Examination revealed the metastatic areas to be firm and white without destruction of bone. Histologically, large, new trabeculae were seen surrounding nests of columnar cell carcinoma as originally seen in the primary tumor in which, according to Stewart, the stroma usually predominates.

2. Osteoclastic: Osteoclastic metastases destroyed normal bone and produced areas of rarefaction. Olin referred to the theory of Stewart that in this type of neoplasm the primary tumor shows a preponderance of medullary cell growth. A combination of osteoplastic and osteoclastic types may appear. Also, the solitary nodular type of metastases may occur in such numbers as to "pepper" the entire bony architecture. Besides the types mentioned, invasion of lymphatic glands and viscera may occur, though they are rarely observed, without bony metastases.

Endothelial Myeloma; Analysis of Cases.—The important features of endothelial myeloma (Ewing's tumor) were presented by Campbell.[20] The data were based on a careful study of 23 cases, 17 of which were registered with the Registry of Bone Sarcoma of the American College of Surgeons. The work of Geschickter and Copeland [21] was referred to frequently, as Campbell compared his observations with those of these authors. He concluded that the nature of the tumor had as yet not been absolutely established, but the structure, he stated, "may approach that of angio-endothelioma, or myeloma." The long bones most frequently affected were the tibia, femur, humerus and fibula, and among the flat bones the pelvis, scapula, clavicle and ribs were most commonly involved. Local metastasis to glands and to the skull were not uncommon. The clinical picture frequently resembled that of acute osteomyelitis or of the sclerosing osteomyelitis of Garré. Four of the 17 patients had been operated on with a diagnosis of osteomyelitis before the true nature of the disease was known.

Angioma of the Spine.—Lièvе [22] summarized 26 cases of angioma of the spine reported in the literature or observed personally. In none of the cases was more than one vertebra involved. The symptoms were those of compression of the cord or nerve roots; local symptoms, though sometimes present, were of a minor nature. Only by means of roentgenograms could a definite diagnosis be made. Compression of the vertebral body was present in only 2 cases. There were irregular areas of diminished density giving a porous, spongy appearance, the

20. Campbell, W. C.: J. Bone & Joint Surg. **16**:761, 1934.

21. Geschickter, C. F., and Copeland, M. M.: Multiple Myeloma, Arch. Surg. **16**:807 (April) 1928; Ewing's Sarcoma: Small Round Cell Sarcoma of Bone, ibid. **20**:246 (Feb.) 1930.

22. Lièvе, J. A.: Presse méd. **42**:1571, 1934.

general density of the whole mass being greater than that of normal bone. The shape of the involved vertebra varied greatly, ranging from a nearly normal size to a markedly increased size and irregularity of contour. Radiotherapy preceded, when necessary by laminectomy gave the best results in ameliorating symptoms and prolonging life.

MYOPATHIES

Glycine Therapy for Various Myopathies.—Tripoli and his co-workers [23] studied the effect of the use of glycine on eleven different pathologic myopathies, including myasthenia gravis, progressive muscular dystrophy, progressive pseudohypertrophic muscular dystrophy, muscular wasting from disuse, progressive spinal muscular atrophy, subacute and chronic poliomyelitis, multiple sclerosis, amyotrophic lateral sclerosis, muscular paralysis from jamaica ginger poisoning, muscular paralysis from peripheral nerve section and Friedreich's ataxia. They found that primary myopathies and myasthenia gravis showed distinct clinical improvement under treatment with glycine and that the inclusion of this amino-acid in the diet increased the appetite and body weight in most of the patients with muscular dystrophy and muscular atrophy.

[ED. NOTE.—The authors have included eleven separate types of myopathies and reported the results of treatment in 43 patients. It seems that the number of patients in each group is too small to allow accurate statements of the results. Several of the editors have used glycine therapy for pseudohypertrophic muscular dystrophy without any striking improvement.]

Chemical Examination of the Muscles in Myasthenia Gravis, Pseudohypertrophic Muscular Dystrophy and Myotonia.—Nevin [24] investigated the phosphorus-holding compounds of muscle in cases of myasthenia gravis, pseudohypertrophic muscular dystrophy and myotonia. He found that the content was normal in patients with myasthenia gravis and concluded that further study of the etiology of this disease should be devoted to an investigation of the excitatory transmission at the neuromuscular junction rather than along metabolic lines. He considered that alterations from the normal observed in muscles of patients with hypertrophic muscular dystrophy and myotonia are due to the degeneration of the muscles and cannot be regarded as a cause of the degeneration. The possible explanations of reported beneficial results following glycine therapy were discussed.

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23. Tripoli, C. J.; McCord, W. M., and Beard, H. H.: Muscular Dystrophy, Muscular Atrophy, Myasthenia Gravis and Strabismus; Clinical and Biochemical Studies of Amino Acid Therapy, J. A. M. A. **103**:1595 (Nov. 24) 1934.

24. Nevin, S.: Brain **57**:239, 1934.

Investigations of the Myopathies.—Paulian [25] examined muscle tissue from 14 patients with primary myopathy. He purposely did not try to classify his cases into different types as he believed that such classifications did not constitute clinical entities and that the so-called pseudohypertrophic juvenile, scapulohumeral and other types all have common characteristics and probably a common origin. His conclusions were that the grouping of the myofibrils in a spiral system and the presence of the nucleus of the muscle in the axis of the fibers suggest embryologic muscular tissue. The presence of histopathologic characteristics of embryonic muscle led him to believe that the myopathies are due to some undetermined change in the growth-regulating mechanism, either primary in the germ plasma or secondary in the endocrine system, which causes a retardation of normal muscle development and a degeneration toward the original embryologic tissue.

INJURIES ABOUT JOINTS

Osteochondritis Dissecans.—Hellström and Ostling [26] reviewed 73 cases of osteochondritis dissecans. In 46 of these the lesion was in the joint of the knee, in 24, in that of the elbow joint; in 1 each, in the first metacarpal and the first metatarsal region, and in 1, in the astragalus. Most of the patients were engaged in heavy labor. Twenty-four per cent of the lesions in the knee and 4 per cent of the lesions in the elbow were in women. In 4 cases the lesions in the knee were bilateral. Both elbows were involved in 2 cases. Three fourths of the cases were in young adults. The usual symptoms were pain on motion and limitation of motion. "Locking" was observed without a foreign body being present. Occasionally capsular thickening or hydrarthrosis was observed. Only 2 patients were free from symptoms when the lesion was discovered; 1 of these had a lesion in the knee, and 1, a lesion in the elbow. The history and the roentgenogram showing the articular structure were of most help in making the differential diagnosis. It was observed that loose bodies shed from the articular surface in some cases increased and in others, decreased in size, and in some became reattached to the articular surfaces or the capsule. The authors concluded that most cases are the result of trauma but that constitutional and hereditary factors predisposed to this disease. Treatment should be expectant for patients who exhibited no symptoms, and the authors advised that in such patients the course of the disease should be closely followed by roentgenograms. They stated that free bodies and necrotic pieces of cartilage which were partially loose should be immediately removed, provided they could be removed without trauma

25. Paulian, D.: Presse méd. **42**:2067, 1934.
26. Hellström, J., and Ostling, K.: Acta chir. Scandinav. **75**:273, 1934.

to surrounding structures. Arthritis deformans developed later in most of the cases.

Loose Bodies in the Elbow Joint.—Kamniker [27] reported 6 cases in which free bodies in the joint limited either flexion or extension. In most instances a traumatic origin from the external condyle was adduced. Indirect trauma pulled off pieces of cartilage, the author believed. Surgical removal was advised.

Injuries to Muscle and Tendon in the Shoulder Region.—Soto-Hall and Haldeman [28] reviewed 86 cases of injuries to muscle and tendon, 40 per cent of which occurred in the shoulder. The cases were classified as follows: tear of the supraspinatus tendon, 13; rupture of the long head of the biceps tendon, 6; rupture of the short head of the biceps tendon, 2; slipping of the long head of the biceps tendon, 2; rupture of the triceps tendon, 2; injury to the rhomboideus major muscle, 6; injury to the latissimus dorsi muscle, 2, and injury to the trapezius muscle, 1. The authors stated that when an acute case of tear of the supraspinatus is suspected the inhibition of function in that tendon as a result of pain in the bursa may be ruled out by injecting 8 or 10 cc. of procaine hydrochloride into the bursa. If the tendon is not affected a full range of abduction of the shoulder becomes possible within a few minutes. The technic of injecting the drug into the bursa was as follows: The needle was directed toward the upper border of the great tuberosity until it struck bone. It was then withdrawn ⅛ inch (0.32 cm.), and an attempt to withdraw fluid within the bursa was made; after this the procaine hydrochloride was injected.

Pathologic Characteristics and Treatment of Sprains.—The functional importance of the areolar tissue filling up the interspaces between the structures surrounding joints was emphasized by Smart [29] in a study of sprains. After sustaining an injury this tissue became edematous, and if the edema was not dispelled a stiffness of the joint resulted. The keynote of recovery after injury to a joint was taken to be the rate and completeness of the absorption of the effusion. The value of electrical stimulation of the muscles controlling the movement of the joint was pointed out.

MISCELLANEOUS

Tetanus Treated with Curare.—Two cases of tetanus in which curare was used were reported by Cole.[30] In both cases the curare

27. Kamniker, K. D.: Deutsche Ztschr. f. Chir. **243**:464, 1934.
28. Soto-Hall, R., and Haldeman, K. O.: California & West. Med. **41**:318, 1934.
29. Smart, M.: Brit. M. J. **2**:673, 1934.
30. Cole, L.: Lancet **2**:475, 1934.

seemed to reduce the continuous rigidity of the muscles of the limbs, abdomen and jaw and to lessen the reflex excitability and the frequency and duration of the spasms. The results were encouraging, but the authors stated that more knowledge regarding the drug and the particular actions of its various alkaloids is required.

Caisson Disease with Pain in the Hip Joints.—After describing the generally known aspect of caisson disease and the incidence of "bends" in his group of patients Christ [31] described what appears to be a new syndrome. So-called "arthritis" has been mentioned by observers before. In four of his patients Christ found a clinical picture of limp, local tenderness in the hip and slight limitation of motion of the hip joint. These patients complained of mild pain. Roentgenograms revealed striking changes in the heads of the femurs of these workers, who were in the third decade of life. Local areas of absorption were present in the cancellous bone of the head of the femur and were followed by a slight secondary arthritic change, but the changes in the head of the femur were doubtless primary. The lesions occurred in workers who had suffered no direct traumas but had worked for years in caissons. Christ expressed the belief that the lesion was probably due to often repeated numerous gas emboli which had eventually damaged the blood supply to local areas in the head of the femur.

Arthralgia and Myalgia Due to the Use of Barbiturates.—Castin and Gardeen [32] reported 6 cases of disorders in the joints due to the use of various forms of the barbiturates. Symptoms were almost entirely subjective, the only objective finding being a slight atrophy of the deltoid muscle in one case. The symptoms, which consisted of pain in the joints and adjacent groups of muscles, were usually limited to a single articulation. The manifestations in the joints came on in the latter part of life. Often the patients had had symptoms of poisoning, such as cutaneous eruptions, digestive disturbances, etc., repeatedly in earlier life, and not until the fourth or fifth decade did symptoms in the joints appear. Roentgen and physical examination gave negative results.

Meniscal Cysts.—In a review of the literature on meniscal cysts, Nicole [33] emphasized the comparative frequency of this lesion. He stated that one cannot always distinguish between the parameniscal and intrameniscal cysts, as Mandl had maintained. The etiology is still a matter of dispute. Nicole stated that a traumatic origin is probably unlikely and that possibly trauma is never the primary cause of meniscal cysts. Taffee's belief that these cysts are truly neoplasms of

31. Christ, A. D.: Deutsche Ztschr. f. Chir. **243**:132, 1934.
32. Castin, P., and Gardeen, P.: Presse méd. **42**:1536, 1934.
33. Nicole, R.: Deutsche Ztschr. f. Chir. **243**:147, 1934.

the joints arising from synovial cells was said to be of interest in this connection. Nicole expressed the belief that constitutional factors may be involved since the lesion nearly always occurs in the second and third decades of life.

[Ed. Note.—Meniscal cysts probably arise from several different causes. Some of them are congenital malformations. One of the editors has observed such cysts in the intra-articular fibrocartilage at autopsy on 2 premature infants.]

The Symphysis Pubis in Women.—Barnes [34] reviewed the anatomy of the symphysis pubis. It was estimated that a force of from 400 to 2,600 pounds (180 to 1,180 Kg.) was necessary to rupture the normal symphysis pubis. Rupture occurred once in from 5,000 to 30,000 deliveries. During pregnancy the relaxation of the symphysis was less than 1 cm. Twenty-six per cent of the multiparas showed widening of the symphysis pubis amounting to 8 mm. or more. Fairly prompt return to normal, the process taking one month, was observed in these cases. Barnes stated that after trauma sustained in childbirth the intra-articular disk of the symphysis may show degenerative changes, and the ligaments, fatty infiltration. According to Barnes, there are many causes of pelvic relaxation and endocrine influences play a major rôle in bringing about such relaxation.

[Ed. Note.—The pelvic articulations in pregnancy [35] have been discussed in the fifty-third and fifty-fifth reports of progress in orthopedic surgery.[36]]

ORTHOPEDIC OPERATIONS

Tuberculosis of the Hip Joint Treated by Fusion Operation.—In a review of the end-results in 170 consecutive unselected cases in which arthrodesis was performed during the period from 1923 to 1931 according to the technic devised by Dr. Hibbs and used in his clinic, Hallock and Toumey [37] reported the following results: 7 patients (4.11 per cent) died within the first postoperative year. Of the 163 patients who survived for more than a year, 68.7 per cent obtained fusion by the first operation. Forty-one patients underwent a second operation; in 26 instances (66⅔ per cent) it was successful. Hallock and Toumey

34. Barnes, J. M.: Am. J. Roentgenol. **32**:333, 1934.

35. Boland, B. F.: New England J. Med. **208**:431, 1933. Abramson, D.; Roberts, S. M., and Wilson, P. D.: Surg., Gynec. & Obst. **58**:593, 1934.

36. Kuhns, John G., and others: Fifty-Third Report of Progress in Orthopedic Surgery, Arch. Surg. **28**:1176 (June) 1934; Fifty-Fifth Report of Progress in Orthopedic Surgery, ibid. **29**:1076 (Dec.) 1934.

37. Hallock, H., and Toumey, J. W., Jr.: Hip Joint Tuberculosis Treated by Fusion Operation; End-Result Study of 170 Unselected Cases, J. A. M. A. **103**: 1836 (Dec. 15) 1934.

considered the factors hindering fusion to be faulty operative technic and faulty immobilization in plaster after operation.

[ED. NOTE.—The article by Hallock and Toumey represents an important study of end-results as their data are based on the largest series of patients with tuberculosis of the hip treated by fusion yet reported. Their observations definitely tend to support the present consensus that the best end-result of treatment of tuberculosis of the hip is a hip fused in good weight-bearing position.]

Disabilities of the Hand Resulting from Loss of Function of the Joint.—In a carefully written article, the troublesome question of loss of function in the hand from limitation of motion in finger joints was considered, and the various procedures available were discussed by Koch.[38] In cases in which the function was only partially limited and the condition had not been of too long standing the best results were obtained by the use of splints and application of well directed physical therapy carried out daily for prolonged periods. Elastic traction with the banjo splint was considered to be of real value if carefully used. Manipulation of the joints under anesthesia usually resulted in limiting rather than improving the power of motion, as the hemorrhage and trauma to the soft tissue resulted in further scarring unless active motion could be begun immediately after the manipulation and carried out faithfully. This was often impossible because of the discomfort immediately following manipulation. Koch called attention to the importance of the collateral ligaments of the finger joints and stated that capsulorrhaphy as advocated by Shaw has been of real value in certain instances. Intra-articular operations, such as arthroplasty, were usually of little value in the small joints of the fingers, as the pathologic changes involved not only the joints but the tendons and other soft tissues. Koch stated that in certain instances arthroplasty of the wrist has been of real value.

Muscular Incisions and Neurotization of Muscles.—Seeman [39] presented his findings concerning neurotization after splitting of the muscle or incisions which divided the nerve supply to the entire muscle or to part of it. He showed that in experimental animals the longitudinal abdominal incision dividing the nerves to the rectus abdominis muscles resulted in permanent paralysis and that in animals with such an incision fat eventually replaced the muscle fibers. Three years after operation no evidence of nerve regeneration was present. Histologic study of portions of human muscle devoid of nerve supply as the result of muscular incisions always showed a high degree of atrophy with

38. Koch, S. L.: Disability of Hand Resulting from Loss of Joint Function, J. A. M. A. **104**:30 (Jan. 5) 1935.

39. Seeman, H. V.: Deutsche Ztschr. f. Chir. **243**:274, 1934.

hyaline degeneration. Replacement of muscle bundles by fat and connective tissue had occurred in places. These principles so often forgotten required restatement, Seeman insisted. He pointed as an example to the muscle-splitting, longitudinal incision into the deltoid muscle: In this muscle the nerves and vessels run at right angles to the muscle fibers, and if the anterior muscle fibers are not to be paralyzed, the incision must be changed. He urged the general use of the incision between the pectoralis major and the deltoid muscle with freeing of the deltoid muscle from the clavicle to enlarge the approach.

[ED. NOTE.—The frequency of paralysis of the anterior portion of the deltoid muscle in the wake of the increasing use of the longitudinal incision splitting the deltoid muscle is of considerable moment. One of us has seen 3 such cases within the past two months; in 2 the incision was made for approaches to the supraspinatus muscle.

Volkmann's Paralysis Treated by Arteriectomy.—Mathieu and his co-workers [40] described a case of Volkmann's paralysis seen three months after onset. The patient had had a supracondylar fracture of the humerus treated by manipulation and application of plaster. Six days later the plaster had been removed because of pain and swelling, and a pressure sore was found in the fold of the elbow. Five weeks later signs of Volkmann's contracture were noted. When seen by the authors the patient presented the typical picture of Volkmann's paralysis with trophic ulcers of the fingers. There was a diminution of sensation but no true anesthesia. Operation was performed, and the brachial artery was found to be obliterated at the elbow joint. Two centimeters of the obliterated portion was resected. After operation the atrophic ulcers of the fingers healed, and four months later the fingers and wrist could be extended almost completely. The authors attributed this improvement to the periarterial sympathectomy that took place when the section of artery was removed. Accordingly they recommended that in early stages not only fasciotomy to release hematomas in the forearm but also sympathectomy of the brachial artery be performed if that vessel is intact, or resection, if it is injured. They stated that in late stages sympathectomy should also be performed either as a means by itself or else as a preliminary to other surgical or conservative treatment of the contractures.

FRACTURES AND DISLOCATIONS

Healing of Fractures of the Neck of the Femur After Osteosynthesis with a Stainless Steel Nail.—Palmer [41] reported the observations at

40. Mathieu, P.; Pedovani, P.; Setille, R., and Norman, P.: Presse méd. **42**: 1819, 1934.

41. Palmer, I.: Acta chir. Scandinav. **75**:416, 1934.

autopsy on a patient aged 70 who died twelve weeks after sustaining a fracture of the neck of the femur which had been immediately nailed with a stainless steel nail. The causes of death were enteritis and bronchitis. In macroscopic and microscopic study of the site of fracture no harmful effects of the nail were seen in the living bone about the nail. There was partial revascularization of the proximal fragment of the femur from the capsule and periosteum. Most of this fragment showed osseous necrosis. Palmer expressed the belief that this form of treatment did not prevent resorptive processes, as shown by the changes in shape and size of the proximal fragment, and that there was risk of displacement. It was necessary to support the hip while healing was taking place.

Report of 631 Fractures of the Neck of the Femur.—Henderson [42] reviewed 631 cases of fracture of the neck of the femur. He tabulated the frequency of union after various surgical procedures for 176 fractures. Manipulation by the Whitman method was successful in 65 per cent of the patients with recent fractures and in 50 per cent of those seen three weeks or more after the original injury. Grafting with a fibular graft driven through the neck of the femur resulted in union in 70 per cent of the patients thus treated. This method proved worthy when tried up to three years after the time of fracture. Beef-bone screws or pegs were used when the operation was performed less than six weeks after the injury, and bony union resulted in 75 per cent of the cases. The Whitman reconstruction operation gave excellent results in 31, and good results in 36, per cent of the cases. The Brackett type of operation was performed in five cases, and the result was satisfactory in each case.

Fractures of the Head of the Tibia.—Becker [43] found that over 70 per cent of a group of fractures of the head of the tibia involved the knee joint. The most common varieties were lateral monocondylar, bicondylar and infracondylar fractures and fracture of the eminentia intercondyloides. He emphasized the egg-shell compression of the surfaces of the joint. The compression, impression and egg-shell fractures were often accompanied by severe meniscal injuries. Becker insisted on exact reposition of the surfaces of the joint. If closed reduction was unsuccessful, he performed an open operation, exposing the joint and removing the meniscus if necessary. He lifted the depressed fragments into place and supported the depressed condyle with a tibial graft if necessary, or held the fragments in place with an ivory peg. Weight bearing was deferred until roentgenograms indicated that the danger of

42. Henderson, M. S.: South. M. J. **27**:1032, 1934.
43. Becker, F.: Deutsche Ztschr. f. Chir. **243**:189, 1934.

recompression seemed past. Mild arthritic changes, mild lateral instability and some limitation of motion were the usual sequelae of the more severe fractures.

Fractures of the Lateral Condyle of the Tibia.—In an analysis of fractures of the condyle of the tibia treated at the Cook County Hospital, Cubbins and his associates [44] reviewed the results of the treatment of 125 fractures of the lateral condyle of the tibia occurring in the past six years. In most cases an attempt was made to secure reposition by molding the fragments and retaining them in a plaster cast. In 50 cases open operation was resorted to with elevation of the depressed fragment and maintenance of its position by the use either of bone chips or of a steel screw with a wooden thread. Cubbins divided these fractures into five types and discussed the method of treatment for each of the various types. He stated that the results have been excellent. There were no severe infections. In one case a screw had to be removed. In no case did ankylosis develop. In every case there was a certain amount of genu valgum, but with more perfect reduction. The amount of knock-knee has been less than in the cases occurring early in the series.

Fractures of the Talus.—Gibson and Inkster [45] studied the mechanism accompanying fractures of the astragalus on the cadaver. It was found that strong dorsiflexion produced eversion of the heel; this was accompanied by rupture of the posterior astragalotibial and posterior tibiocalcaneal fibers of the deltoid ligament and of the medial fibers of the interosseous (astragalocalcaneal) ligament, successively. On a fresh specimen a similar manipulation caused the astragalus to appear between the stretched tendons of the flexor longus hallucis on one side, and the tendons of flexor longus digitorum and tibialis posterior on the other. The tendo Achillis assumed a position lateral to the midline. The mechanism of fracture without dislocation was thought to be produced by forced dorsiflexion beyond normal limits with the line of strain passing through the metatarsal shafts and the cuneiform and navicular bones to the head of the astragalus, and it was believed that any part of this line may give way. If the force continues without any of these parts giving way, the tibia, at its anterior joint line, acts as an apex of a wedge fracturing the neck and pushes the body backward sometimes through the "buttonhole" formed by the flexor tendons. The prognosis was generally regarded as bad, with convalescence requiring many months, and Gibson and Inkster stated that according to some writers

44. Cubbins, W. R.; Conley, A. H.; Callahan, J. J., and Scuderi, C. S.: Surg., Gynec. & Obst. **59**:461, 1934.

45. Gibson, A., and Inkster, R. G.: Canad. M. A. J. **31**:357, 1934.

recovery is never complete. Treatment varies with each case. The authors stated that crushing of the anterior part of the bone can be corrected by manual remodeling, followed by rest in splints, and later by the use of an iron stabilizing apparatus with a T strap. When the body of the bone is crushed a subastragalar arthrodesis may be required to bring about alinement of the foot and leg. When the posterior fragment is displaced backward, reposition of the fragments (provided the blood supply is adequate) and partial or total astragalectomy are the methods available. The authors expressed the belief that partial astragalectomy is unsatisfactory. Case histories of 3 patients who had sustained injury to the astragalus without displacement, and of 3 who had sustained fractures with displacement, of the posterior fragment were given.

Study of End-Results of Fractures of the Shaft of the Humerus.—Rogers [46] analyzed the end-results of 82 fractures of the shaft of the humerus treated at the Massachusetts General Hospital between 1925 and 1931; fractures through the surgical neck, supracondylar and pathologic fractures were excluded. Satisfactory results were obtained in 80 per cent of the cases; in 20 per cent the results were relatively unsatisfactory. In the groups in which the patients were confined to bed better end-results were obtained than in groups in which the patients were ambulatory. Rogers concluded that when fractures of the shaft of the humerus are treated intelligently by any suitable method, the end-results are excellent. Generally, transverse fractures should be reduced by manipulation (closed or open) and held by fixation (external or internal). Oblique fractures should be reduced and held by constant traction. And comminuted fractures should be treated by the simplest method suited to the individual case. Constant traction was found to be dangerous. (The device most commonly used was a Thomas arm splint or a Blake suspension with the arm in abduction, the elbow at a right angle and the forearm suspended vertically in transverse or short oblique fractures, especially in the lower and middle thirds.) Traction with the patient in bed (with a Thomas arm splint or a Blake suspension) was always more effective than that with the patient ambulatory (the latter traction may be applied by means of a Jones humeral splint). Open reduction was found necessary only in cases in which nonunion and failure to accomplish satisfactory reduction by closed methods were anticipated. Bone plating alone after bone repair had subsided was found not to bring about secondary union, but it brought about such union in fresh fractures or in those in which bone grafts were used. Nonunion was frequently found in a transverse and short oblique fracture in the middle and lower thirds of the humerus when there had

46. Rogers, H.: Surg., Gynec. & Obst. **59**:934, 1934.

been no contact between the ends of the bone during the period of active repair, which was usually considered to last two weeks. Injury to the radial nerve rarely resulted in permanent disability if a cock-up splint was worn and physical therapy was given to the extensor groups of muscles.

Epiphysiolysis of the Proximal End of the Radius.—Von Oppolzer[47] attempted closed reduction of fractures of the head of the radius. Eight cases were recounted, successful reposition resulting in each. The maneuver used with the patient under anesthesia may be briefly described as follows: The elbow was extended with the forearm supinated. The elbow was bent into a varus position over the operator's knee, and traction was made on the forearm, increasing the space between the neck of the radius and the external condyle. Then the dislocated head was pushed and manipulated with the thumb, mostly from behind, while the forearm was slowly flexed or pronated. Most of the reductions occurred during the pronation. A nonpadded plaster splint was worn for three weeks.

Treatment of Fractures of the Carpal Scaphoid.—For treatment of delayed nonunion of the carpal scaphoid, Soto-Hall and Haldeman[48] recommended that the bone be exposed through a dorsoradial incision and drilled across the line of fracture. Subsequently the fractures were treated as were fresh fractures of the scaphoid, i. e., by immobilization of the thumb and hand in plaster at from 30 to 40 degrees of dorsal flexion and complete radial deviation for from seven to nine weeks. Of 7 cases of delayed union, 5 ended in union after this procedure. Of 16 fractures of the scaphoid 75 per cent resulted in union after immobilization in plaster in the position described. In cases in which there were nonunion and marked deformity total excision of the bone followed by immobilization in plaster in extreme ulnar deviation for from five to six weeks was recommended.

RESEARCH

Cause of Death in Cases of Fat Embolism.—Rückert[49] stated that, aside from direct cerebral and cardiac lesions, death of patients with fat embolism is due chiefly to renal lesions. In fact, retention uremia experimentally induced is much like cerebral fat embolism in its clinical aspects. He stated that the literature contains conflicting reports on the alterations of the nonprotein nitrogen after intravenous injection of fat into the blood stream. He therefore gave injections to a series of 10 rabbits and 3 dogs and found that small doses of fat given by slow

47. von Oppolzer, R. R.: Deutsche Ztschr. f. Chir. **243**:427, 1934.
48. Soto-Hall, R., and Haldeman, K. O.: J. Bone & Joint Surg. **16**:822, 1934.
49. Rückert, W.: Deutsche Ztschr. f. Chir. **243**:537, 1934.

intravenous injection raised the nonprotein nitrogen moderately. Large intravenous doses (5 cc.) administered rapidly raised the nonprotein nitrogen markedly and in three days led to death with the picture of uremia and cerebral fat embolism. Fat from bone marrow and petrolatum acted similarly. If small doses (from 1 to 2 cc.) were injected directly into the renal arterial supply of a dog the nonprotein nitrogen rose, and if 4 cc. was used the figures rose to fatal levels. Fat injected into the abdominal aorta of a rabbit in doses of 2 cc. caused a rise of 352 mg. of nonprotein nitrogen followed by death of the animal.

Infection in Cases of Avitaminosis, with Special Reference to the Occurrence of Acute Osteomyelitis.—Attempts were made by Takahashi [50] to study groups of animals fed on diets lacking the vitamins, to determine the sites of localization of intravenously injected staphylococci. The animals which received food deficient in vitamin A showed a diminished resistance as compared to controls, but exhibited no particular involvement of the muscles. In those which received food lacking in vitamin C metaphyseal lesions in bones frequently developed, while no such lesions occurred in control animals. Doubtless the circulatory disturbances visible in the metaphyses in the animals not receiving vitamin C predisposed to involvement in these regions.

Assimilation of Phosphorus from Di-Calcium Phosphate, Tri-Calcium Phosphate, Bone Di-Calcium Phosphate and Cooked Bone Meal.—Three experiments were carried out by Rottensten and Maynard [51] with rats. The phosphorus intake was kept at a minimum level, and the calcium-phosphorus ratio was held constant in the diets under comparison. In the first experiment the effects of di-calcium phosphate and cooked bone meal were compared, growth and development of bone being used as the criteria. In the second experiment chemically pure di-calcium phosphate, bone di-calcium phosphate and chemically pure tri-calcium phosphate were used. In the third experiment the effects of bone di-calcium phosphate and cooked bone meal were studied on female rats carried from weaning through their first lactation. In all these experiments the usefulness of the supplements was shown by the data for ash content of the bones. In the last experiment it was observed not only that the weight of the young rats receiving the supplement exceeded that of the young of other rats but that in the bones of those rats both the percentage and the amount of ash remained higher than in those of the controls which did not receive supplement; a higher level of inorganic phosphorus was also shown in the blood. There was a slightly increased amount of evidence in favor of a secondary over a

50. Takahashi, R.: Arch. f. klin. Chir. **181**:103, 1934.

51. Rottensten, K. V., and Maynard, L. A.: J. Nutrition **8**:715, 1934.

tertiary phosphate, but the difference was too slight to warrant its use in practice.

Experimental Infarction of the Femur in Rabbits.—In an attempt to produce experimental lesions of the upper end of the femur in rabbits, Kistler,[52] using rabbits of various ages, injected a 2 per cent suspension of charcoal into the nutrient arteries supplying the upper end of the femur and observed the changes occurring after the lapse of varying lengths of time. He was able to produce definite infarcts of the metaphysis and to follow the reparative changes and subsequent vascularization. He was of the opinion that production of these nutritional disturbances demonstrated conclusively that the vascular system of the upper end of the femur in rabbits is closed. He also noted pathologic changes in the epiphysis and in the region of the epiphyseal line similar to those found clinically in patients with Legg-Perthes' disease. Nutritional disturbances produced in this way affected the rate of growth as well as the rate of ossification of the femur. Areas of increased density in the infarcts were found to be due to deposition of inorganic calcium salts.

Fractures of the Neck of the Femur, Dislocations of the Hip and Obscure Vascular Disturbances Producing Aseptic Necrosis of the Head of the Femur.—In a careful clinical roentgenologic and pathologic study of injury to the upper end of the femur Phemister [53] correlated the pathologic changes which occurred. He found that intracapsular fracture of the neck of the femur by injuring the blood supply resulted in aseptic necrosis of a part or all of the head of the femur and that such occurrences increased the likelihood of nonunion of the fracture. The presence of aseptic necrosis could usually be diagnosed by roentgenograms taken two or three months after injury and was characterized by areas of increased density which represented portions of necrotic bone and by areas of decreased density which represented processes of creeping substitution. According to Phemister, the articular cartilage may also become necrotic and be absorbed or replaced by fibrocartilage or connective tissue. Months or years may be required for completion of the change. He stated that it is important to recognize this process clinically and to protect the softened bone from too great weight bearing during the period of transformation in order to prevent collapse of the normal architecture with resultant deformity and impairment of the functional result. He pointed out the fact that similar changes representing aseptic necrosis occurred in certain instances of slipping of the upper epiphysis of the femur, traumatic dislocation of the hip, the

52. Kistler, G. H.: Sequences of Experimental Infarction of Femur in Rabbits, Arch. Surg. **29**:589 (Oct.) 1934.

53. Phemister, D. B.: Surg., Gynec. & Obst. **59**:415, 1934.

reduction of congenital dislocations of the hip, and arthroplasty for the mobilization of ankylosed hips. He attributed the changes in these cases to interference with the circulation supplying nutrition to the head of the femur and expressed the belief that this interference also caused the aseptic necrosis seen in cases of Legg-Perthes' disease, but he pointed out that so far no single factor such as trauma, embolism, infection, etc., offered an adequate explanation for the pathologic process seen in these cases.

[ED. NOTE.—This article represents observations and deductions gathered from a large collection of clinical cases and from careful studies of pathologic changes in excellent specimens. It helps to clarify the pathologic picture seen in a variety of conditions and points the way toward a more rational treatment.]

Studies in Sarcoma of Bones.—In an effort to stimulate formation of new bone in tumor tissue Brunschwig and Harmon [54] injected calcium in various forms into the tissue of transplanted rat tumors in 37 instances. Viosterol was also given by mouth. In no case, however, was there formation of new bone, which furnished evidence against the hypothesis that bone in osteogenic sarcoma, or its metastasis, is merely the result of a mesoblastic tumor in proximity to a supply of calcium. The experiments also demonstrated that calcium could not produce osteogenic properties in malignant mesoblastic cells if such properties were not already exhibited by these cells.

Rôle of Bone and Endosteum in Regeneration of Bone.—In experiments on 6 dogs McGaw and Harbin [55] resected a section of fibula with periosteum and in the defect thus created inserted curettings of bone marrow and endosteum from the opposite tibia. In all the animals there was regeneration of bone, and in from twenty-one to twenty-nine days there was a distinct homogeneous callus. In sixty days a medullary cavity was established, and in all the animals the new bone was well fused to the shaft of the fibula.

Experimental Regeneration of Bone with Lime Salts and Autogenous Grafts as Sources of Available Calcium.— Dogs were used in an experimental study by Stewart [56] to verify the findings of Murray.[57] In each instance grafts of boiled bone died when inserted into defects of the radius; furthermore, there was no production of new bone about or within those defects. The only source available for the formation of new bone was from the ends of the radius. When lime salts were implanted in radial defects there was failure of regeneration of the

54. Brunschwig, A., and Harmon, F. H.: Am. J. Cancer **22**:342, 1934.
55. McGaw, W. G., and Harbin, M.: J. Bone & Joint Surg. **16**:816, 1934.
56. Stewart, W. J.: Surg., Gynec. & Obst. **59**:867, 1934.
57. Murray, C. R.: Ann. Surg. **93**:463, 1931.

shaft. Small fragmented live grafts similarly used or small chips of bone accidentally left behind at operation consistently showed growth of new bone in large amounts. When traumatized muscle and lime salts were mixed and placed in the radial defect a few areas of calcification were seen, but no regeneration of the shaft occurred. Proliferative arthritis resulted from implantation of lime salts in carpal and tarsal defects, but no new bone was laid down after such implantation.